AUTISM IN FEMALES

Emma Saure
Master's Thesis
Master 's Programme in Neuroscience
Department of Biosciences
November 2018
Supervisors: Maija Castrén
and Juha Salmitaival

Tiedekunta – Fakultet – Faculty Faculty of Biological and Environmental Sciences		Koulutusohjelma – Utbildingsprogram – Degree Programme Master's Programme in Neuroscience
Tekijä – Författare – Author Emma Saure		
Työn nimi – Arbetets titel – Title Autism in females		
Oppiaine/Opintosuunta – Läroämne/Studieinriktning – Subject/Study track Neuroscience		
Työn laji – Arbetets art – Level Master's Thesis	Aika – Datum – Month and year November 2018	Sivumäärä – Sidoantal – Number of pages 77

Tiivistelmä – Referat – Abstract

Background and objectives: Autism spectrum disorders (ASD) are developmental neuropsychiatric disorders in which core symptoms are problems in communication and interaction as well as restrictive and repetitive behaviour and interests. ASD is 2-5 times more common in males than in females. In recent years, researchers have found, that there are differences between females and males in ASD symptoms, neuropsychological characteristics, comorbid problems, neurobiology and etiology. The purpose of this systematic review is to give a comprehensive picture about the role of female sex/gender in ASD. To establish this, the review covers symptoms of autism, neuropsychology, neurobiology, comorbidity, neurogenetics and neuroendocrinology. Research questions were the following: 1) Is there evidence of sex/gender differences in ASD symptoms and comorbidity disorders? 2) Are there sex/gender differences to be found in ASD etiology? 3) What kind of support different explanations about sex/gender bias have gotten in various research areas? The purpose of the study is also to integrate the existing theories into one model that takes account to different aspects of sex/gender differences in ASD.

Methods: The protocol of this systematic review follows "The Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) when applicable. Eligibly criteria and search terms were selected in a way that would offer the widest range of articles covering the subjects of this study. Literature search was conducted using the Medline and PsychINFO as search engines. The final sample consisted of a total of 129 articles. Data was extracted on all relevant variables of the study, that were the number of participants, age of participants, specific diagnoses, methods and results.

Results: Sex/gender differences in ASD were found in all areas that were included in this systematic review. Females with high function ASD (HFASD) were found to have less problems in social communication and interaction and less repetitive and restricted behavior and interests than males with HFASD. In addition, HFASD were found to have better language skills than males with HFASD. However, females with ASD were found to have more sensory processing problems, mental health problems and epilepsy than males with ASD. Females with ASD were also found to have lower full-scale intelligence quotient than males with ASD. In the context of etiology, it has been found that there are sex/gender differences in neuroanatomy, susceptibility genes and hormone levels.

Conclusions: Results from this systematic review suggest that females with HFASD are underdiagnosed. This results from etiological sex/gender differences that cause partially different clinical presentation of ASD between females and males. ASD research has also concentrated mostly on males with ASD while ignoring females with ASD. Underdiagnosing can have many unfavorable consequences for females with HFASD since if they do not have a diagnosis, they do not get support. In the future, it is crucial to pay attention to females with ASD in the clinical work and scientific research.

Avainsanat – Nyckelord – Keywords autism spectrum disorder, gender differences, sex differences, neuroscience, neuropsychology, genetics, endocrinology
Ohjaaja tai ohjaajat – Handledare – Supervisor or supervisors Maija Castrén, Juha Salmitaival
Säilytyspaikka – Förvaringställe – Where deposited E-thesis
Muita tietoja – Övriga uppgifter – Additional information

Tiedekunta – Fakultet – Faculty Bio- ja ympäristötieteellinen tiedekunta		Koulutusohjelma – Utbildingsprogram – Degree Programme Neurotieteen maisteriohjelma
Tekijä – Författare – Author Emma Saure		
Työn nimi – Arbetets titel – Title Autismi naisilla		
Oppiaine/Opintosuunta – Läroämne/Studieinriktning – Subject/Study track Neurotiede		
Työn laji – Arbetets art – Level Maisterintutkielma	Aika – Datum – Month and year Marraskuu 2018	Sivumäärä – Sidoantal – Number of pages 77

Tiivistelmä – Referat – Abstract

Tutkimuksen tausta ja tarkoitus: Autismi on kehityksellinen neuropsykiatrinen häiriö, jonka keskeisiä oireita ovat vaikeudet sosiaalisessa vuorovaikutuksessa ja kommunikaatiossa sekä toistava ja rajoittunut käyttäytyminen ja kiinnostuksen kohteet. Autismi on noin 2-5 kertaa yleisempi miehillä kuin naisilla. Viime vuosina on huomattu, että autismi voi ilmetä hieman eri tavoin naisilla kuin miehillä. Tämän systemaattisen katsauksen tarkoitus oli muodostaa kattava kokonaiskuva autismista naisilla, minkä vuoksi tutkimus kattoi seuraavat autismin osa-alueet: oireet, liitännäisongelmat, neuropsykologiset piirteet, neurobiologian, neurogenetiikan ja neuroendokrinolgian. Tutkimuskysymykset olivat seuraavat: 1) Onko autismin kliininen kuva naisilla erilainen kuin miehillä? 2) Onko autismin etiologiasta löydettävissä sellaisia eroja naisten ja miesten välillä, mitkä voivat selittää sukupuolivinoumaa? 3) Onko sukupuolivinoumaa selittäville tekijöille löydettävissä todisteita ja onko selityksiä mahdollista yhdistää yhdeksi kokoavaksi teoriaksi? Lisäksi tarkoitus on muodostaa malli, joka kokoaa aikaisemmat teoriat yhdeksi kokonaisuudeksi.

Menetelmät: Tutkimus toteutettiin systemaattisena katsauksena, jossa seurattiin PRISMA-ohjetta soveltuvin osin. Katsaukseen valittavien artikkelien kriteerit ja käytetyt hakusanat määriteltiin niin, että tuloksena saataisiin mahdollisimman kattavasti artikkeleita, joissa käsitellään tutkimuksen aiheita. Artikkeleita haettiin PsycINFO- ja MedLine-tietokannoista. Kriteerit täyttäviä artikkeleita löytyi yhteensä 129 kappaletta. Artikkeleista kerättiin tutkimuksen kannalta oleelliset tiedot, joita olivat osallistujien määrä, ikä, sukupuoli ja diagnoosityyppi, käytetyt menetelmät ja tulokset.

Tulokset: Sukupuolieroja löytyi kaikilta tutkimuksen kohteena olevilta alueilta. Autismikirjon naisilla, joilla on normaali kognitiivinen kapasiteetti, on havaittu olevan vähemmän vaikeuksia sosiaalisissa tilanteissa sekä vähemmän toistavaa ja rajoittunutta käyttäytymistä ja kiinnostuksenkohteita kuin autismikirjon miehillä. Lisäksi heillä todettu olevan paremmat kielelliset taidot kuin autismikirjon miehillä. Poikkeavuuksia aistiärsykkeiden prosessoinnissa autismikirjon naisilla on sen sijaan löydetty enemmän kuin autismikirjon miehillä. Autismikirjon naisilla on havaittu myös olevan enemmän mielenterveyden ongelmia ja epilepsiaa kuin autismikirjon miehillä. Lisäksi autismikirjon naisilla on havaittu olevan matalampi kognitiivinen peruskapasiteetti kuin autismikirjon miehillä. Etiologian osalta sukupuolieroja on löydetty neuroanatomiasta, alttiusgeeneistä ja hormonitasoista.

Johtopäätökset: Tutkimustulokset viittaavat siihen, että autismia ei tunnisteta naisilla riittävän hyvin. Syynä tähän ovat sukupuolierot autismin etiologiassa, jotka ovat johtaneet siihen, että autismin oirekuva on osittain erilainen miehillä ja naisilla. Autismitutkimus on myös keskittynyt pääasiassa autismikirjon miehiin. Alidiagnosoinnilla on monia negatiivisia seurauksia autismikirjon naisille, koska ilman diagnoosia he eivät saa tarvitsemaansa tukea. Tulevaisuudessa on erityisen tärkeää kiinnittää sekä tutkimuksessa että kliinisessä työssä huomiota myös autisminkirjon naisiin.

Avainsanat – Nyckelord – Keywords
Autismi, sukupuolierot, neurotiede, neuropsykologia, genetiikka, endokrinologia

Ohjaaja tai ohjaajat – Handledare – Supervisor or supervisors
Maija Castrén, Juha Salmitaival

Säilytyspaikka – Förvaringställe – Where deposited
E-thesis

Muita tietoja – Övriga uppgifter – Additional information

Table of contents

Abbreviations used in this study in order of appearance:

ASD =autism spectrum disorder
FSIQ = full scale intelligent quotient
DSM-V = Diagnostic and statistical manual of mental disorders, fifth edition
DSM-IV = Diagnostic and statistical manual of mental disorders, fourth edition
HFASD = high functioning autism spectrum disorder
LFASD = low functioning autism spectrum disorder
NT = neurotypical
ID = intellectual disability
MNDs = minor neurological dysfunctions
PRIMSA = the preferred reporting items for systematic reviews and meta-analyses
RRBI = repetitive and restricted behavior and interests
VIQ = verbal intelligence quotient
NVIQ = nonverbal intelligence quotient
MRI = magnetic resonance imaging
fMRI = functional magnetic resonance imaging
EEG = electroencephalography
CNVs = copy number variants
SNPs = single nucleotide polymorphisms

1. Introduction

1.1. Autism spectrum disorder

Autism spectrum disorder (ASD) is a neurodevelopmental condition in which core symptoms are deficits in social communication and interaction as well as repetitive and restricted behavior and interests. Prevalence of ASD in recent estimations is 1–2 % (Baio et al., 2018; Christensen et al., 2016; Idring et al., 2015) and ASD is evaluated to be 2-5 times more common in males than females (Baio et al., 2018; Kirkovski et al., 2013; Rivet & Matson, 2011b; Rutherford et al., 2016; Van Wijngaarden-Cremers et al., 2014). This sex/gender bias has been an enigma since Kanner (1943) noticed that ASD is predominantly a disorder of males. The biased sex/gender ratio has also lead researchers to have mostly male participants in studies. In recent years, researchers have found, that there are differences between females and males in ASD symptoms, neuropsychological characteristics, comorbid problems, neurobiology and etiology (Haney, 2016; Kirkovski et al., 2013; Lai et al., 2017; Schaafsma & Pfaff 2014; Werling & Geschwind 2013) and nowadays there is a growing interest towards the role of sex and gender in ASD. The purpose of this systematic review is to give a comprehensive picture about the role of female sex/gender in ASD. Due to the multifactorial nature of ASD, it is critical to cover broad evidence spanning from symptoms of autism, to neuropsychology, neurobiology, comorbidity, neurogenetics and neuroendocrinology. Based on this multilevel data perhaps a more integrated picture of the autism in females can be formed.

The latest diagnostic system, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) defines autism as a unified spectrum disorder that is wide and variable. According to DSM-V, persistent deficits in social communication and social interaction across multiple contexts are required for the diagnosis of ASD (American Psychiatric Association, 2013). To fulfill the diagnostic criteria, these deficits manifest in the three different areas as follows: 1) social-emotional reciprocity, 2) nonverbal communication behaviors that are used for social interaction, and 3) developing, maintaining, and understanding relationships (American Psychiatric Association, 2013). Additional core diagnostic criteria for ASD include restricted, repetitive patterns of behavior, interests, or activities in at least two of the following domains: 1) stereotyped or repetitive motor movements, use of objects, or speech, 2) insistence on sameness, inflexible adherence to routines, or ritualized patterns of verbal or nonverbal behavior, 3) highly restricted, fixated interests that are abnormal in intensity or focus, or 4) hyper- or hyporeactivity to sensory input or unusual sensory interest (American Psychiatric Association, 2013). In DSM-V, ASD is

divided into three categories that are separated by how much support an individual with ASD needs. These categories are independent of full scale intelligence quotient (FSIQ).

In the previous Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 2000) ASD refers to many different diagnoses. In articles that are referred in this review, ASD is used to refer Asperger's disorder, autistic disorder and pervasive developmental disorder not otherwise specified. Most of the articles do not specify the number of participants by different diagnosis but rather use only the term ASD for all these diagnoses. In DSM-V, as discussed above, all these diagnoses are also combined under one category. All of these diagnoses also have the same core symptoms, but the range of symptoms as well their severity can vary between autistic disorders. Since most of the articles referred to this review have used only ASD to refer all of them and DSM-V also combines all previously made diagnosis under ASD, this term it is used this way also in this review.

ASD is usually divided into high- and low-functioning ASD (see for example reviews Chen et al., 2017; Kirkovski et al., 2013; Rubenstein et al., 2015; Werling & Geschwind 2013). High functioning autism spectrum disorder (HFASD) refers to individuals with FSIQ 70 or over and low functioning autism spectrum disorder (LFASD) refers individuals with IFSQ 69 or lower. It should be noted that the level of functioning does not necessarily reflect the severity of ASD symptoms. However, the age at which ASD diagnosis is made correlates with the severity of symptoms of ASD and whether a person has HFASD or LFASD. Those who get diagnosis early in life, have more severe symptoms, more intellectual and language disabilities and parents have higher concerns about initial symptoms (Daniels & Mandell 2014; Giarelli et al., 2010; Shattuck et al., 2009). ASD can also occur with or without intellectual and/or language impairments, and in some cases, it can be associated with some other neurodevelopmental, mental or behavioral disorder, or catatonia (American Psychiatric Association, 2013). To conclude, ASD is used in this review in accordance with the new DSM-V system to refer to the autism spectrum that is wide and heterogeneous.

1.2. Neuropsychological, neurobiological, and etiological background

In this section, neuropsychological deficits, neurobiological abnormalities, comorbid disorders, as well as heritability and endocrinological abnormalities in ASDs are introduced shortly to provide context on how these could relate to gender and sex.

Language impairments are a typically co-occurring with ASD. Problems in language development are often among the earliest signs of ASD (Mody & Belliveau 2013). ASD is also

commonly associated with suprasegmental language problems such as deficits in perceiving and producing prosody (Mody & Belliveau 2013; Paul et al., 2005). Furthermore, those ASD individuals who do not have delayed or impaired language can have many subtle problems in language processing. Particularly processing of complex auditory information can result in impaired and/or atypical performance in ASD (O'Connor 2012). Processing of complex auditory information can be difficult in situations with background noise. In addition, autism may be accompanied with altered orientation to auditory stimuli and deficits in perceiving prosodic features (O'Connor 2012). Language can also display other problems such as restricted and repetitive behavior. For example, as echolalia that refers to unsolicited repetition of some phrases (American Psychiatric Association, 2013).

Many executive function deficits are associated with autism: weak central coherence, cognitive inflexibility, problems of response inhibition, and attention deficits (see reviews Craig et al., 2016; Happé & Frith 2006; Sanders et al., 2008). It is suggested, that neuropsychological deficits are directly related to ASD symptoms and some neuropsychological dysfunctions correlate with neuroanatomical alterations that are observed in ASD individuals (Sander et al., 2008). Weak central coherence, meaning that attention is driven to details and there are problems of integration details into a meaningful global picture, is suggested to be associated with problems in social situations (Happé & Frith 2006). Cognitive inflexibility and deficits in inhibition are thought to be related to repetitive and restricted behavior (Hill, 2004; Sanders et al., 2008). To conclude, ASD is associated with many neuropsychological deficits.

Emotion recognition problems and prosopagnosia (face blindness) are generally observed in individuals ASD (Uljarevic & Hamilton 2013; Weigelt et al., 2012). The identification of emotion and faces is essential for successful social interaction. ASD individuals are generally worse than neurotypicals (NT) in recognizing face identity (Weigelt et al., 2012). Especially face memory is impaired (Weigelt et al., 2012). Numerous studies have also reported difficulties in emotion recognition in ASD (see review Uljarevic & Hamilton 2013). It is suggested, that problems of emotion recognition cause profound difficulties in social development and therefore could even be the primary deficit in ASD (Hobson et al., 1986). Emotion recognition deficits are shown to be independent of age and FSIQ (Uljarevic & Hamilton 2013).

Comorbid psychiatric diagnoses are common among ASD individuals: about 60–70% of individuals with ASD have at least one co-occurring psychiatric condition and often more than one comorbid diagnosis coexists (Amr et al., 2012; Simonoff et al., 2008). Depression, anxiety, fears, self-injurious behavior, schizophrenia, ADHD, challenging behavior, and eating disturbances are common comorbid conditions with ASD (Amr et al., 2012; Råstam 2008; Simonoff et al.,

2008). Some comorbid problems are associated with specific symptoms of ASD. Atypical sensory processing is associated with fears, picky eating and self-injurious behavior (Cermak et al., 2010; Duerden et al., 2010; Råstam 2008). Anxiety and depression, in turn, can be promoted by fatigue and stress caused by attempts to adjust to society mainly designed by NTs and by feeling different and lonely (Lai et al., 2017b; Livingston et al., 2018). In addition to psychiatric diagnoses, comorbid neurological conditions are also frequently observed in ASD. Epilepsy is more common in ASD individuals than in general population. The risk is particularly increased in ASD individuals with intellectual disability (ID) (Amiet et al., 2008). According to a meta-analysis, the prevalence of epilepsy is 21.4% in ASD participants with ID and 8% in ASD participants without ID (Amiet et al., 2008). Minor neurological dysfunctions (MND) have been observed even in 74% of children with ASD (De Jong et al., 2011).

Neurobiological abnormalities are often found in ASD. Since Kanner (1943), many studies have reported higher risk for macrocephaly as indexed by larger head circumference. Later brain imaging studies have also reported increased total brain volume (see reviews Ecker et al., 2015; Stanfield et al., 2008). Enlargement of brain seems to be specifically observed in young children with ASD, being no longer present around the age of 6–8 years (Ecker et al., 2015). Numerous studies have also found atypical cortical gyrification (Ecker et al., 2015). There are also abnormalities in both regional brain activity as well as brain connectivity in ASD (see reviews Philip et al., 2012; Traves et al., 2012). Results from studies that measure task-related activity patterns are heterogeneous, but in general it seems that individuals with ASD recruit at least partially different brain areas than NTs (Philip et al., 2012). ASD is also generally associated with brain hypoconnectivity (Ecker et al., 2015). Most consistent findings of altered connectivity have been observed in the corpus callosum, cingulum and some parts of the temporal lobe (Travers et al., 2012). ASD is also associated with atypical white matter tracts (Travers et al., 2012).

ASD has a high heritability, estimates varying between 64–91% (Tick et al., 2016). At least 1000 genes are known to be associated with ASD (Ayhan & Konopka, 2018). There are both rare and common genetic variants that are associated with increased risk of ASD. Many genetic developmental disorders are associated with ASD, for example fragile X-syndrome, tuberous sclerosis and neurofibromatosis type 1 (Persico & Napolioni 2013). Also, many psychiatric and neuropsychiatric conditions, like schizophrenia, have overlapping susceptibility genes with ASD (Anney et al., 2017). At least several hundred genes with de novo mutations increase the risk of ASD (Iossifov et al., 2014; Persico & Napolioni 2013; Sebat et al., 2007). Many of the genes that are associated with ASD regulate biological pathways that are involved in brain development and functioning (Ayhan & Konopka, 2018). These genes affect, for example, activity-dependent

signaling, neuron growth and neuronal migration (Persico & Napolioni 2013). Genes that are involved in regulation of oxytocin and vasopressin, hormones that affect social behavior, are also associated with ASD (Fakhoury 2018). Genetic influence of the X chromosome is also thought to be crucial for ASD susceptibility (Marco & Skuse 2006). ASD is more common in people who have an atypical number of X-chromosomes, for example, Klinefelter syndrome in which male have sex chromosomes XXY (Cederlöf et al., 2014). Interestingly, excessive numbers of Y chromosome increase the risk and severity of ASD even more than excessive numbers of X chromosome (Tartaglia et al., 2017). However, both rare and common gene variations that are associated with ASD are located in the X chromosome (Chen et al., 2017; Nava et al., 2012). Furthermore, during gestation, sex chromosomes have a crucial role in the regulating of hormones that are suggested to be involved in the development of ASD Schaafsma & Pfaff 2014).

Besides genetics, hormonal factors associated with ASD have been examined with endocrinological methods. Testosterone is suggested to have a role in development of ASD (Baron-Cohen et al., 2011). Testosterone affects brain development during the prenatal period and sex/gender differences in testosterone levels are involved in sex/gender differences of empathy, emotional intelligence, visuospatial abilities and verbal communication (Durdiakova et al., 2011). Some studies have found that fetal exposure to testosterone correlates with ASD traits in normal population (Ayeung et al., 2009b; Knickmeyer et al., 2006). Also altered levels of oxytocin and vasopressin, which affect social behavior, are frequently reported (Dumais et al., 2016). Oxytocin levels are lower in ASD individuals than NTs and oxytocin and vasopressin levels correlate with symptoms of ASD (Oteify et al., 2018; Zhang et al., 2016). A low oxytocin level correlates positively with social difficulties whereas a low vasopressin level correlates with repetitive and restricted behavior in ASD individuals (Zhang et al., 2016). Some clinical trials have found that intranasal oxytocin improves emotion recognition and increases amygdala activation during face processing, providing initial evidence that oxytocin might be a candidate for treatment of some ASD features (Domes et al., 2013; Guastella et al., 2010).

In conclusion, ASD has been researched from many points of views and there are many problems that can be associated with ASD as well as many etiological causes. As described below, each of these viewpoints could be relevant for providing deeper understanding of the autism in females. These different areas of research are summarized in the Figure 1.

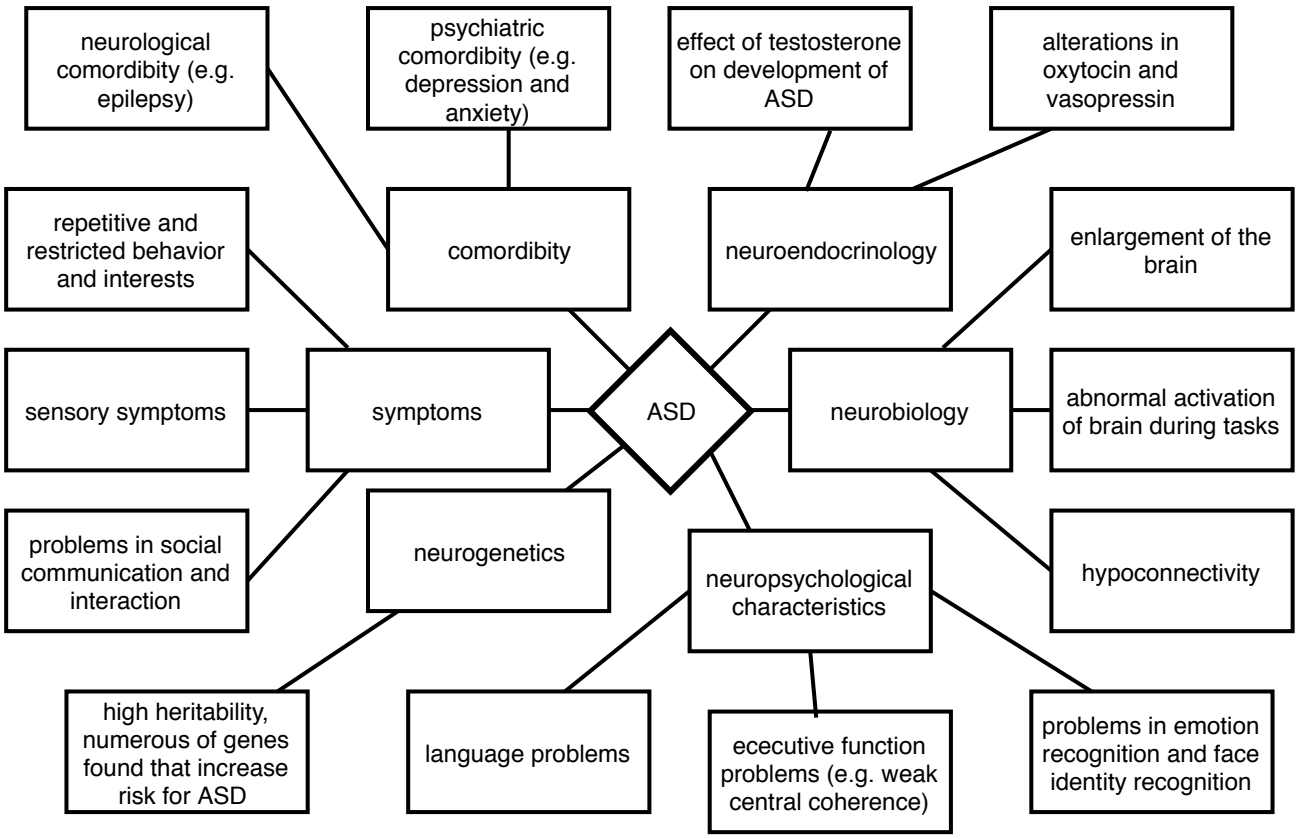

Figure 1. ASD research areas.

1.3. Autism spectrum disorder in females

The question of gender and sex differences in ASD relate to several practical and theoretical questions. It is widely discussed whether ASD is underdiagnosed in females. Solving this question requires deeper understanding of how ASD is manifested in females. The biased sex ratio has also encouraged the search for the causes of male predominance. There are theories suggesting etiological reasons causing males to be more susceptible for ASD than females. In this section, the concepts of sex and gender are first defined and after that different theories about sex/gender bias in ASD are introduced.

Sex refers to biological traits, like chromosomes and hormone levels. Gender, in turn, is a psychological characteristic related to personal identity and behavior. Since subjective experience of gender-related issues and gender-identity begins to form in interaction with the environment immediately after birth, it is difficult to separate effects of sex and gender. Because of this, both sex and gender are used when discussing about these issues in this review. Some research suggest that sex/gender are rather a continuum than binary categories (Ainsworth 2015). However, since sex/gender are categorized as male and female in all relevant research articles that are included in this systematic review, this binary classification is adopted here.

The underdiagnosis of females with ASD is suggested to amplify the male preponderance. One possible cause for the underdiagnosing of females is related to the autism screening tools, which are developed based on a typical picture of male symptoms that has been biased by differential gender rations in the studies validating diagnostic criteria (Haney, 2016). Previous reviews suggest that HFASD females may have less repetitive and restricted behavior and interests than males and they adapt better to social situations than males (Kirkovski et al., 2013; Van Wijngaarden-Cremers 2014). The hypothesis about underdiagnosing is supported by notions of the bias in male-female ratio, especially among HFASD. Female-male ratio in ASD is estimated to be around 1:2-5 (Baio et al., 2018; Kirkovski et al., 2013; Saemundsen et al., 2013; Sun et al., 2014; Van Wijngaarden-Cremers et al., 2014), but according to a recent meta-analysis, that takes into account the possibility of underdiagnosing females the ratio is closer to 1:3 (Rutherford et al., 2016). Similar ratio has been found in studies that screened prevalence of ASD in general population, and not only studies including participants that already had an ASD diagnosis (Oliveira 2007; Saemundsen et al., 2013; Sun et al., 2014).

There are many theories about etiological differences among females and males with ASD. Some studies suggest that there is a "female protective effect" against autism (Robinson et al., 2013; Skuse et al., 2000). This theory is supported by some genetic studies that have found a greater mutational burden in females with ASD than in males with ASD (Jacquemont et al., 2014) and also by the findings that in the LFASD group females have generally lower FSIQ than males (see review Rivet & Matson 2011a). This could mean that females have a higher threshold to develop ASD. The specific mechanism of such a female protective effect is unknown. However, X-chromosomes are thought to be involved in female protective effect, as females have two X-chromosomes compared to only one in males (Skuse et al., 2000). During the early embryonic development, one X-chromosome normally inactivates randomly. If there is a mutation in the X-chromosome, the inactivation could be skewed towards the healthy X-chromosome and protect females from ASD since genes in the inactivated chromosome are not expressed (Edens et al., 2011; Schaafsma & Pfaff 2014).

Autism has also been suggested to represent "extreme male brain" (Baron-Cohen, 2002). This point of view originates from the typical thinking styles in autism, which resemble extreme version of stereotyped cognitive patterns of males. Empathizing refers to the ability to identify other's mental states, emotions and thoughts and to respond to these with accurate emotions. Systemizing refers to the ability to analyze how complex systems work and understanding different rules that determine the behavior of systems. The name "extreme male brain" comes from the observation, that in general females are better in empathizing and males are

better in systematizing and therefore ASD is seen as a version of an extreme male thinking style. This theory is also supported by studies reporting correlations between testosterone levels and ASD symptoms (Ayeung et al., 2009b; Knickmeyer et al., 2006). Since males have in general higher testosterone levels support the theory that ASD represents an extreme version of typical male characteristics.

On the contrary to the extreme male brain theory, some researchers have suggested that there is abnormal gender coherence (less gender typical features than usual or features that resemble other gender more than assigned gender) that is observed both in females as well as in males (Bejerot et al., 2012). This theory is supported by studies that have found abnormal gender coherence in neuroanatomy and in sex/gender specific anthropometric traits in ASD (Bejerot et al., 2012; Ecker et al., 2017). Also, in general population, ASD traits are correlated positively with androgynous face features (Gilani et al., 2015). In conclusion, it is clear that sex/gender bias occurs in ASD, but both the extent as well as the cause of this bias is still controversial. Currently there are three key theories trying to explain sex/gender bias from different point of views and the evidence is scattered. Hence, a systematic review aiming to integrate this evidence is clearly needed.

1.4. Study questions and hypothesis

Study questions and hypotheses are as following:

1. Is there evidence of sex/gender differences in ASD symptoms and comorbid disorders? Based on previous reviews, it was hypothesized that the reported evidence will point to less restrictive and repetitive behavior and interests (RRBI) in females with HFASD than males with HFASD (see reviews Kirkovski et al., 2013; Rubenstein et al., 2015; Van Wijngaarden-Cremers et al., 2014; Werling & Geschwind 2013). Also, it was hypothesized that among LFASD, accumulated evidence would support that females have more symptoms than males (see review Amiet et al., 2008; Rivet & Matson 2011a).

2. Is there evidence of sex/gender differences in ASD etiology? Based on previous reviews and theoretical articles, it was hypothesized that some evidence of sex/gender differences in neuroanatomy, susceptibility genes and hormone levels among ASD individuals will be found (see reviews Carter 2007b; Chen et al., 2017; Werling & Geschwind 2013). However, due to the heterogeneity of the studies, it was difficult to predict what will be the most consistent findings.

3. What kind of support different explanations and theories get from the existing body of evidence related to ASD in females across various research areas? It was hypothesized, that evidence will be found for each main theory, but none of the existing theories can cover the findings regarding sex/gender differences comprehensively. The purpose of the study is also to integrate the existing theories into one model that takes account to different aspects of sex/gender differences in ASD.

2. Methods

2.1. Protocol

The protocol of this systematic review followed "The Preferred Reporting Items for Systematic reviews and Meta-Analyses" (PRISMA) when applicable (Liberati et al., 2009). More specifically, eligibly criteria, search strategy, study selection, data collection and evaluation of limitations and biases was defined and performed according PRISMA protocol.

2.2. Eligibly criteria

The following inclusion criteria were used to select relevant articles for review: a) articles published in English language and in a peer-reviewed journal, b) original articles that reported studies of females with autism spectrum disorder (ASD) and results of ASD females that were compared to those of males with ASD or neurotypical females and specifically separated the effects of sex /gender, c) articles reported results from at least one of the following areas of ASD research: symptomology, neuropsychology, comorbidity, neurobiology, neurogenetics or neuroendocrinology, d) data in the article was analyzed statistically. No limitations regarding to the age, severity of ASD or IQ of the participant were included.

2.3. Search procedure

The literature search was conducted using the Medline and PsychINFO as search engines. Search terms were 1) autism spectrum disorder or Asperger syndrome and 2) sex differences or gender differences or sex-specific. All searches were conducted in February 14th, 2018. To include all

essential articles, the review articles that were identified in the initial search were also screened for relevant references and the grey literature was subjected to a separate search by Google Scholar using the specified search terms. Based on these additional searches, 30 additional articles were identified.

2.4. Study selection

The literature search resulted in 667 articles. After removal of duplicates, altogether 555 articles that were screened by title and abstracts. At this stage, 340 articles were excluded. The remaining 215 articles were then screened based on full text, which led to the exclusion of additional 86 articles. The final sample thus included 129 articles. A flowchart of the study selection process is presented in Figure 2.

2.5. Data extraction

One hundred twenty-nine articles that fulfilled the eligibly criteria were divided to six predefined categories: symptoms, neuropsychology, comorbidity, neurobiology, neurogenetics and neuroendocrinology. Data were extracted on all relevant variables of the study (see Table 1). Numbers of articles and participants for each category are described in Table 1. See also Supplementary Tables 1–17, describing the participants, methods and main results of every article included this review. If one article reported data in two or more categories that article was included in the multiple categories section.

2.6. Data analysis

Data was analyzed based on information collected from articles (see Supplementary Tables 1-17). Meta-analysis was performed of a subgroup of studies to confirm results that were found in the qualitative analysis of studies. Review Manager 5.3 (2014) was used to conduct meta-analysis. In the neurobiology sub-domain, data available from studies that reported MNI or Talairach coordinates were combined into a brain map in case sex/gender differences in ASD were reported. The map was created with BrainMap software (Fox & Lancaster 2002). Additionally, data of those studies that reported sex/gender specific genetic association and linkages in ASD, was included in the picture of chromosomes. The picture was drawn with CyDas (Hiller et al., 2004).

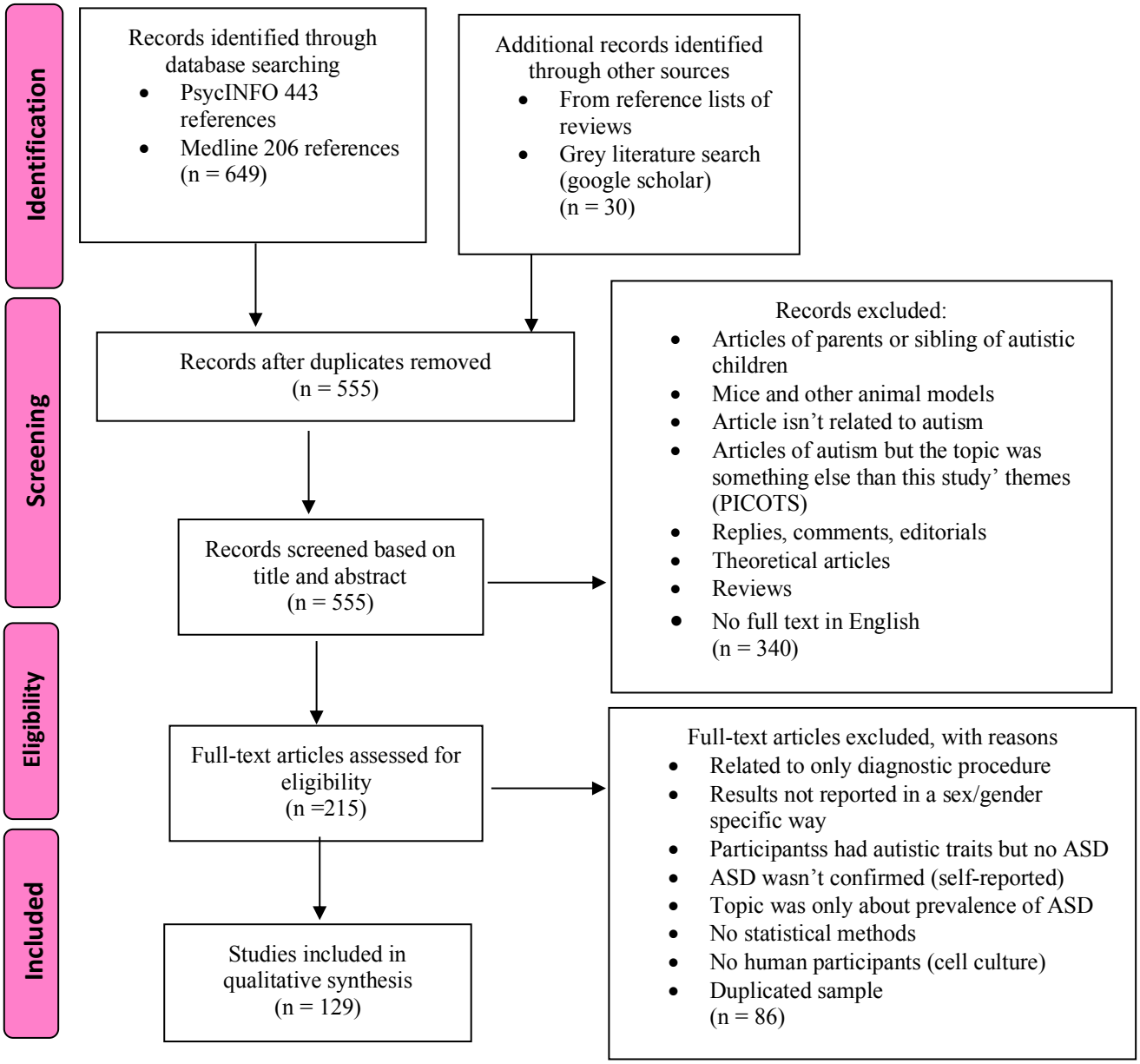

Figure 2. Flow chart of study selection.

Table 1. The number of articles and participants in each category.

Category	Subcategory	Number of articles	Number of participants				Extracted data
			ASD F	ASD M	NT F	NT M	
Symptoms	Social communi-cation and interaction	42	2692	8178	1824	1712	p-values and cohen's d (if available) of comparisons in different questionnaires or diagnostic procedures
	Restrictive and repetitive behavior and interest	33	2143	7268	448	327	p-values and cohen's d (if available) of comparisons in different questionnaires or diagnostic procedures
	Sensory symptoms	7	271	654	-	-	p-values and cohen's d (if available) of comparisons in different questionnaires
Neuro-psychology	Cognitive ability	13	1104	5803	-	-	Intelligence quotient and p-values and cohen's d (if available) about comparisons
	Language	13	655	3114	156	205	p-values and cohen's d (if available) of comparisons in different test or questionnaires (e.q. non-word repetition verbal fluency)
	Executive functions	9	314	560	109	99	p-values and cohen's d (if available) of comparisons in different test or questionnaires
	Emotion and face recognition	7	508	525	538	295	p-values and cohen's d (if available) of comparisons in different test (e.g. emotion and face regonizition)
	Empathizing and systemizing	8	633	833	4203	2823	p-values and cohen's d (if available) about comparisons EQ and SQ questionnaires
Comorbidity	Psychiatric comorbidity	25	1362	4962	1508	1505	p-values and cohen's d (if available) of comparisons in different questionnairesor data collected from medical records
	Neurological comorbidity	5	221	943	139	98	p-values and cohen's d (if available) of comparisons of neurological examination or questionnaire or magnetic resonance imaging
Neurobiology	Brain structure and functioning	18	366	543	333	377	Magnetic resonance imaging coordinates, p-values from comparisons of volume of different brain areas or brain activity comparisons
	Brain connectivity	5	132	197	185	216	p-values of brain connectivity comparisons
Neuro-genetics	Genetic burden	4	45 twin pairs, 915 families, 1547375 females, 1619827 males				Heritability and recurrence rates, mutational burden
	X-chromosome	3	4709 families, 212 ASD females, 865 NT females				Information about X-chromosome skewedness
	Association and linkage studies	17	10637 families, 2989 ASD, 4082 NT				Gene association and linkages
Neuro-endocrinology	Testosterone	6	543	121	738	67	p-values of comparisons of testosterone and related levels and testosterone related issues
	Oxytocin and vasopressin	1	19	21	16	19	p-values of comparisons of oxytocin and vasopressin levels

ASD=autism spectrum disorder, NT=neurotypical, F=females, M=male

3. Results

3.1. Symptoms

3.1.1. Deficits in social communication and interaction

Among studies with HFASD, most of the studies found sex/gender differences in social communication and interaction (see Figure 3). It is reported that females with HFASD appear to use more camouflaging and masking and they may be able to cope with their social deficits better than males (Dean et al., 2017; Lai et al., 2017b; Ormond et al., 2018). Camouflaging was operationalized by comparing external behavior in social situations to internal state, for instance, social cognitive capacity (Lai et al., 2017) and masking was measured by parental perception of their children's behavior (Ormond et al., 2018) or by comparing discrepancy between observed ASD symptoms and observed behavior in playground situation (Dean et al., 2017). Females with HFASD also reported to exhibit more joint engage (Dean et al., 2017), use of more gestures (Rynkiewicz et al., 2016), and prosocial behavior (Mandy et al., 2012; Sedgewick et al., 2016), make rarely inappropriate discussion initiations (May et al., 2016), have better friendship skills (Baron-Cohen and Wheelwright, 2003a; Head et al., 2014) and are more accepted by peers (Dean et al., 2014) than males with ASD. Some studies also found that females with HFASD have better social communication and interaction skills overall than males with HFASD (Lai et al., 2011, 2012, 2013, 2017; Park et al., 2012). Altogether, 14 of 22 studies reported that females with HFASD have less problems in social communication and interaction than males with HFASD. See Table 2 for the number of participants. Other studies, altogether 7 of 22, have not found sex/gender differences in social deficits among HFASD individuals (Banach et al., 2009; Bölte et al., 2011; Coffman et al., 2015; Holtmann et al., 2007; Kumazaki et al., 2015; Solomon et al., 2012; Supekar et al., 2015; Szatmari et al., 2012; White et al., 2017). Only one study with HFASD participants found that females have greater social difficulties than males (Grove et al., 2017). However, these findings were based on Autism Quotient, which is a self-assessing method. Therefore, it is possible that the results are not as reliable as those of other studies which are mostly based on evaluation by an experienced health care practitioner. Meta-analysis of studies which investigated sex/gender differences in social communication and interaction among HFASD and provided results in numeric values confirms that females with HFASD have less problems in social communication and interaction than males with HFASD ($p<.001$) (see Figure 3).

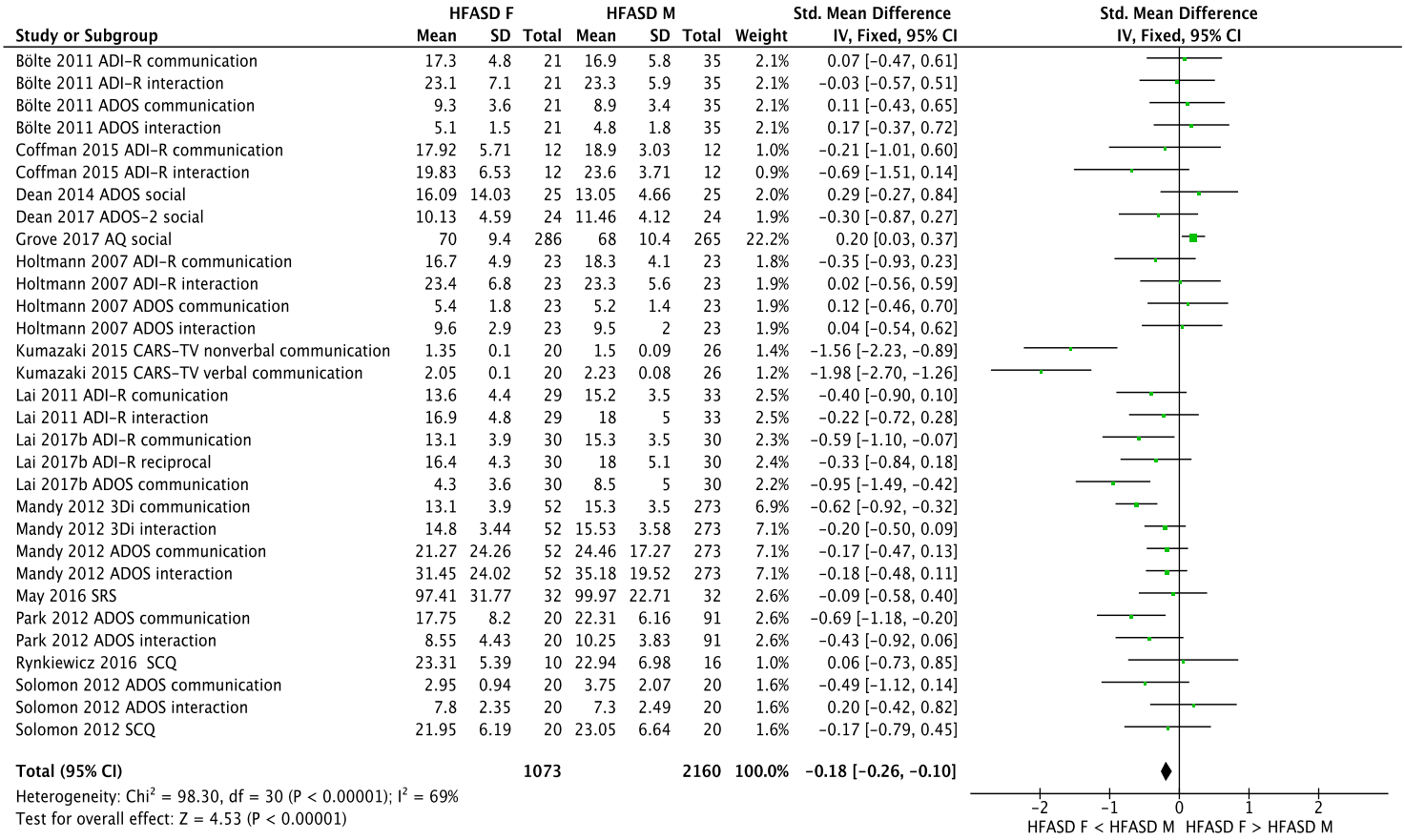

Figure 3. A meta-analysis of studies that investigated differences in social communication and interaction between females with HFASD and males with HFASD. Females with HFASD have less problems in social communication and interaction than males with HFASD (p<.001). Abbreviations: 3Di= The Developmental, Dimensional and Diagnostic Interview, ADOS=Autism Diagnostic Observation Schedule, ADI-R: Autism Diagnostic Interview-Revised, AQ= Autism Quotient, CARS-TV= Childhood Autism Rating Scale, SCQ=Social Communication Questionnaires SRS=Social Responsiveness Scale.

Studies that have both HFASD and LFASD participants have reported mixed results. Some studies found that females with ASD have less problems in social interaction and communication than males with ASD (Backer van Ommeren et al., 2017; McLennan et al., 1993; Sedgewick et al., 2016) whereas other studies found that females with ASD have more problems in social interaction and communication than males with ASD (Frazier et al., 2014; Wang et al., 2017). Most of the studies that have both HFASD and LFASD participants showed no sex/gender differences in social interaction and communication (Banach et al., 2009; Fulton et al., 2017; Harrop et al., 2015a; Øien et al., 2018; Reinhart et al., 2015; Rivet & Matson 2011b; Sipes et al., 2011; White et al., 2017).

Among LFASD participants, most studies found, that females with LFASD have more social deficits than males with LFASD (Carter et al., 2007a; Hartley and Sikora, 2009; Konstantareas et al., 1989; Tsai and Beisler, 1983; Wang et al., 2017), but some studies did not find differences in social communication and interaction between females and males with LFASD

(Mandic-Maravic et al., 2015; Mussey et al., 2017; Postorino et al., 2015; Rivet & Matson 2011b). See Table 2 for number of participants of these studies. Meta-analysis of studies which investigated sex/gender differences in social communication and interaction among LFASD and provided results in numeric values confirms that females with LFASD have more problems in social communication and interaction than males with LFASD (p<.001) (see Figure 4).

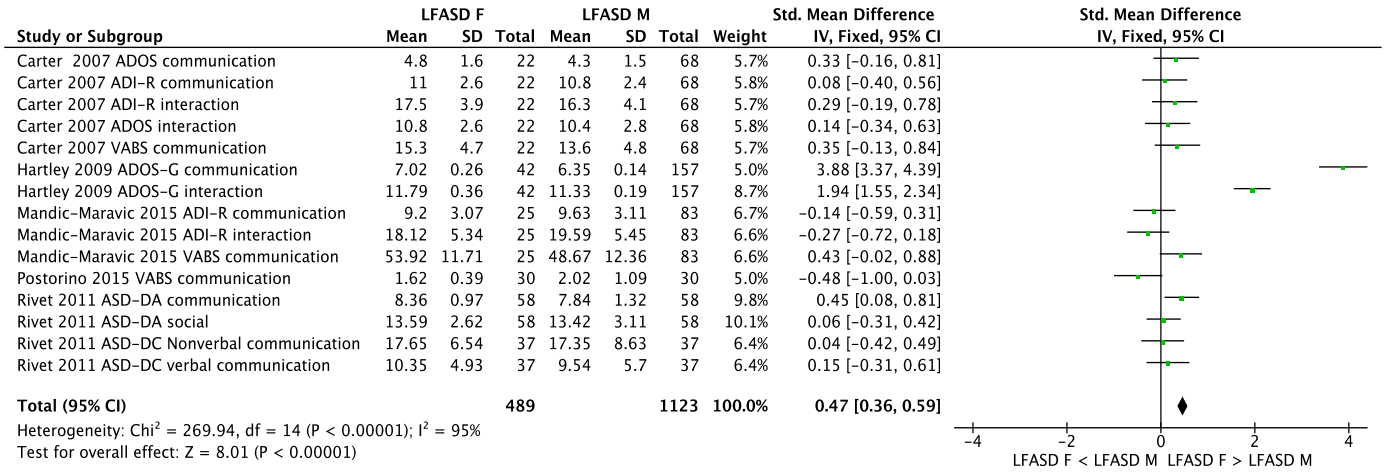

Figure 4. A meta-analysis of studies that investigated differences in social communication and interaction between females with LFASD and males with LFASD. Females with LFASD have more problems in social communication and interaction than males with LFASD (p<.001). Abbreviations: ADOS= Autism Diagnostic Observation Schedule, ADI-R=Autism Diagnostic Interview-Revised, VABS= Vineland Adaptive Behavior Scales.

Table 2. The number of studies and participants that reported sex/gender differences in social communication and interaction among ASD participants. Studies are categorized according to the level of functioning participants.

Problems in social interaction and communication	ASD Females > ASD Males Studies/participants	ASD Females < ASD Males Studies/participants	ASD Females = ASD Males Studies/participants
HFASD /mainly HFASD	1/551	14/1303	7/2290
Studies that included both HFASD and LFASD or participants functioning level was not told	2/3482	3/211	8/1585
LFASD /mainly LFASD	6/453	0/0	4/1037

Age may have effects on the occurrence of sex/gender differences in social deficits (see Table 3). In studies with ASD children less than 10 years old, most of the studies did not find sex/gender differences in social deficits (Banach et al., 2009; Fulton et al., 2017; Harrop et al., 2015a; Kumazaki et al., 2015; Mandic-Maravic et al., 2015; Postorino et al., 2015; Øien et al., 2018; Reinhart et al., 2015; Rivet & Matson 2011b; Sipes et al., 2011; Szatmari et al., 2012) whereas many studies that have adolescent or adults as participants found that females with ASD have less problems in social communication and interaction than males with ASD (Backer van Ommeren et

al., 2017; Head et al., 2009; Lai et al., 2011, 2012, 2013, 2017; McLennan et al., 1993; Pisula et al., 2018; Sedgewick et al., 2016).

Table 3. The number of studies and participants that reported sex/gender differences in social communication and interaction among ASD participants. Studies are categorized according to the age of the participants. Table does not include two studies that have an age scale too wide to be categorized according to age (Mussey et al. 2017; McLennan et al. 1993).

Problems in social interaction and communication	ASD Females > ASD Males Studies/participants	ASD Females < ASD Males Studies/participants	ASD Females = ASD Males Studies/participants
Children (under 12y)	4/831	6/367	13/3664
Adolescent (about 10-18 y)	1/2418	5/586	4/379
Adults (over 18y)	1/551	5/265	1/116

In conclusion, studies suggest that among individuals with HFASD, females have better social skills than males. Among individuals with LFASD, in turn, it is possible that females may have more social deficits than males, although the evidence of such differences is not consistent. There is also currently no evidence of sex/gender differences in social communication and interaction among children with ASD. However, adolescent and adult females with ASD appear to have less social deficits or they use more camouflaging and coping than same-aged males with ASD.

3.1.2. Repetitive and restricted behavior and interests (RRBI)

Among studies in individuals with HFASD, 14 out of 17 studies have found sex/gender differences in RRBI (see Figure 5). These studies have suggested that females with HFASD have less routinized and stereotypic play (Mandy et al., 2012), repetitive motor movements (May et al., 2016), repetitive speech (May et al., 2016), restricted interests (Solomon et al., 2012), and overall RRBI symptoms than males with HFASD (Bölte et al., 2011; Coffman et al., 2015; Kumazaki et al., 2015; Lai et al., 2011, 2012, 2013, 2017; Park et al., 2012; Sipes et al., 2011; Supekar et al., 2015; Szatmari et al., 2012). Three studies found no sex/gender differences in RRBI among HFASD (Dean et al., 2014, 2017; Holtmann et al., 2007). See Table 4 for the numbers of participants in individual studies. See also Figure 5 which presents a meta-analysis, that included all studies which investigated sex/gender differences in RRBIs among HFASD and provided numeric values of measurement. This analysis also confirms that females with HFASD have less RRBIs than males with HFASD ($p<.001$)

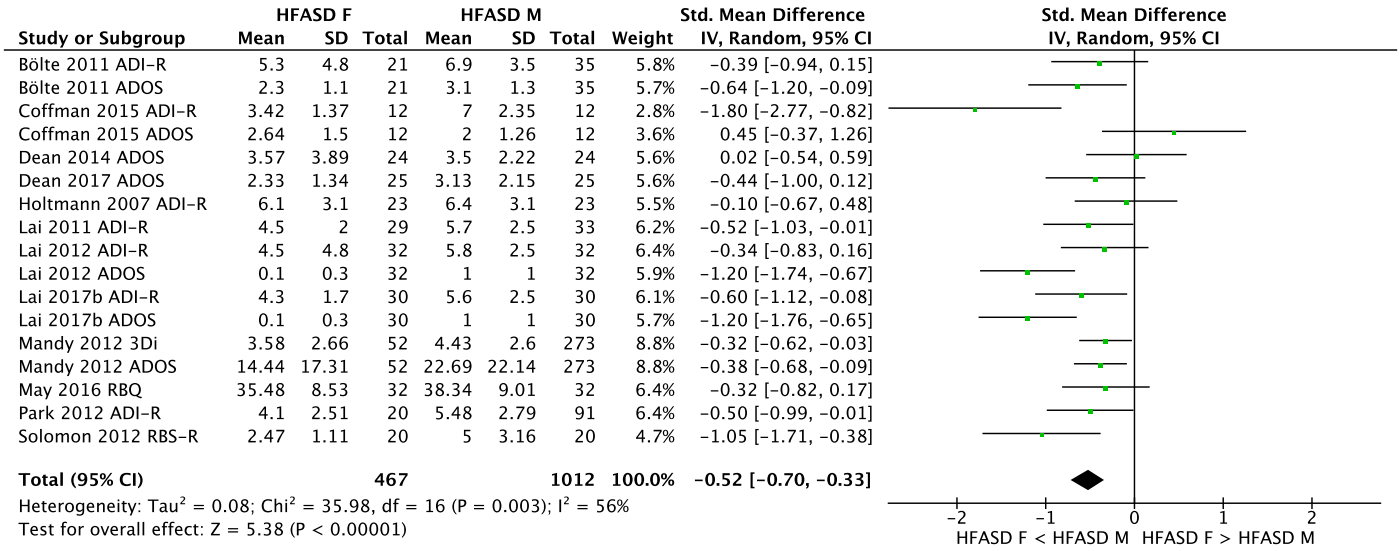

Figure 5. A meta-analysis of studies that investigated differences in social communication and interaction between females with LFASD and males with LFASD. Females with LFASD have more problems in social communication and interaction than males with LFASD (p<.001). Abbreviations: ADOS= Autism Diagnostic Observation Schedule, ADI-R= Autism Diagnostic Interview-Revised, RBQ= Repetitive Behavior Questionnaire, RBS-R= Repetitive Behavior Scale–Revised.

Among the studies that included both LFASD and HFASD participants or studies that did not separate LFASD or HFASD the results are inconsistent. One study found, that females have less repetitive use of objects, interests in of parts of objects and repetitive speech (Wang et al., 2017). They also found, that females had more stereotyped hand and finger mannerism than males, but still females with ASD had less overall RRBI than males with ASD (Wang et al., 2017). Another study found that females with ASD have less restricted interest, stereotypy and total RRBI than males with ASD (Frazier et al., 2014). Most of the studies that have both HFASD and LFASD participants found no sex/gender difference in RRBI (Banach et al., 2009; Joseph et al., 2013; McLennan et al., 1993; Øien et al., 2018; Reinhardt et al., 2015; White et al., 2007). See Table 4 for the number of studies and participants.

Among studies with LFASD participants the results are inconsistent. Some studies found that females with LFASD have less repetitive and unusual visual interests (Harrop, et al., 2015b; Lord et al., 1982), less stereotypic behavior (Hattier et al., 2011), routinized and stereotypic play (Lord et al., 1982), restricted interest (Frazier et al., 2014) and overall RRBI (Hartley et al., 2009) than males with LFASD (see Table 4). Other studies failed to find differences in RRBI between females and males with LFASD (Carter et al., 2007a; Mandic-Maravic et al., 2015; Postorino et al., 2015; Rivet & Matson, 2011b; Sipes et al., 2011).

Table 4. The number of studies and participants reporting sex/gender differences in RRBI among ASD participants. Studies are categorized according to the level of functioning of participants.

Restrictive and repetitive behavior and interest	ASD Females > ASD Males Studies/participants	ASD Females < ASD Males Studies/participants	ASD Females = ASD Males Studies/participants
HFASD /mainly HFASD	0/0	14/3100	3/144
Studies that included both HFASD and LFASD or participants functioning level was not told	0/0	2/3482	7/1066
LFASD /mainly LFASD	0/0	4/872	5/739

It is also possible, that age affects occurrence of sex/gender differences in RRBI (see Table 5). It seems, that there is a tendency that the sex/gender difference becomes more pronounced in later life. Most of the studies of adolescent or adult participants have found that females have less RRBI (Bölte et al., 2011; Hattier et al., 2011; Lai et al., 2011, 2012, 2013, 2017; Mandy et al., 2012; May et al., 2016; Solomon et al., 2012; Supekar et al., 2015). Among children with ASD the results are inconsistent. Many studies in which participants are under 12 years old did not find sex/gender differences in RRBI (Banach et al., 2009; Carter et al., 2007a; Dean et al., 2014, 2017; Joseph et al., 2013; Mandic-Maravic et al., 2015; Postorino et al., 2015; Øien et al., 2018; Reinhart et al., 2015, Rivet & Matson 2011b) whereas other studies found that females with ASD have less RRBI than males with ASD (Coffman et al., 2015; Harrop et al., 2015b; Hartley et al., 2009; Kumazaki et al., 2015; Lord et al., 1982; May et al., 2016; Park et al., 2012; Szatmari et al., 2012; Wang et al., 2017)

Table 5. The number of studies and participants that reported sex/gender differences in ASD in social communication and interaction. Studies are categorized according to age of participants. Table does not include one study (McLennan et al., 1993) that had too wide an age range to be categorized according to age. Also, another study reported mixed results inside the same age group but was divided according to the level of functioning was also excluded here (Rivet et al., 2011; Sipes et al., 2011).

Restrictive and repetitive behavior and interest	ASD Females > ASD Males Studies/participants	ASD Females < ASD Males Studies/participants	ASD Females = ASD Males Studies/participants
Children (under 12y)	0	9/4069	10/1015
Adolescent (about 10-18 y)	0	5/2889	2/283
Adults (over 18y)	0	5/405	1/116

In summary, studies in HFASD females suggest less RRBI than those in males but in LFASD studies sex/gender differences are not clear. Age may also have an effect on the occurrence of sex/gender differences in RRBI, meaning that among children the results are inconsistent but adolescent and adult females have less RRBIs than males.

3.1.3. Sensory processing

Most of the studies that investigated sex/gender differences in sensory processing reported that females have more sensory symptoms than males (see Figure 6). It has been reported that females with HFASD have more sensory symptoms than males with HFASD. Such findings have been reported both in adults (Lai et al., 2011) and in children (Kumazaki et al., 2015; Ormond et al., 2018). One of these studies found that females with HFASD especially dislike some odors and they avoid situations where these odors occur (Kumazaki et al., 2105). However, two studies found no sex/gender differences in sensory symptoms among HFASD (Mandy et al., 2012; Park et al. 2012).

One study that had both HFASD and LFASD participants reported also that females with ASD have more sensory symptoms than males with ASD (Amr et al., 2011). However, another study that had both HFASD and LFASD participants suggested that females have less unusual sensory sensitivities than males (Øien et al., 2018). There were no studies that compared sex/gender differences in sensory sensitivities among LFASD participants.

To conclude, 4 out of 7 studies suggest that females with ASD have more sensory symptoms than males with ASD. A meta-analysis confirmed that females with ASD have more sensory symptoms that males with ASD ($p<.001$). The meta-analysis included all studies that investigated sex/gender differences in sensory processing and provided results in numeric values (see Figure 6). It should be noted, however, that there was considerable variability in the questionnaires that were used in individual studies, and usually there were only few specific questions specifically addressing sensory symptoms. Nevertheless, the results from this limited body of research clearly suggest that females have more sensory symptoms, but the results should be considered preliminary.

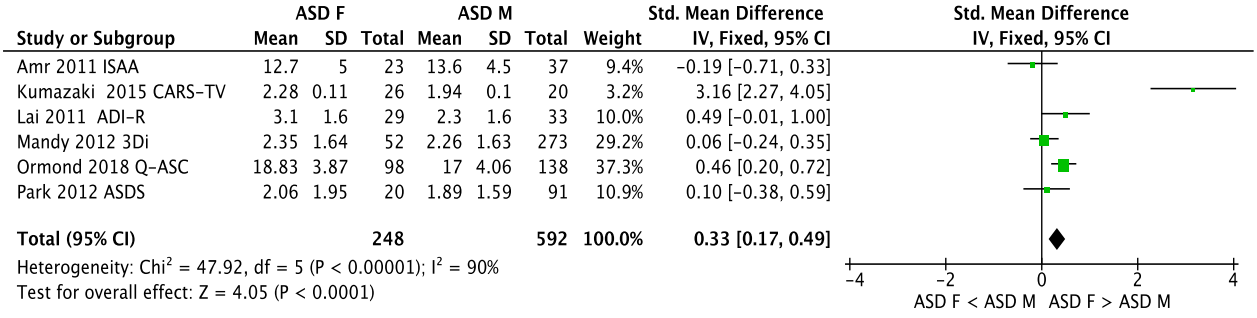

Figure 6. A meta-analysis of studies that investigated sensory processing differences between females with ASD and males with ASD. Females with ASD have more sensory processing problems than males with ASD ($p<.001$).
Abbreviations: 3Di= The Developmental, Dimensional and Diagnostic Interview, ADI -R=Autism Diagnostic Interview-Revised ASDS= Asperger's Syndrome Diagnostic Scale, CARS-TV= Childhood Autism Rating Scale, ISAA= Indian Scale for Assessment of Autism, Q-ASC= The Questionnaire for Autism Spectrum Conditions.

3.2. Neuropsychology

3.2.1. Cognitive ability

Many studies have found that females with ASD have on average lower full-scale IQ (FSIQ) than males with ASD. Some studies have found that females with ASD have lower FSIQ (Frazier et al., 2014; Tsai and Beisler, 1983) and nonverbal IQ (NVIQ) (Ankeman et al., 2014; Frazier et al., 2014; Lord et al., 1982) verbal IQ (VIQ) (Backer van Ommeren et al., 2017; Frazier et al., 2014) than males with ASD. One study found, that among families that have only one child with ASD, females had lower FSIQ than males, but among families that have more than one child with ASD, there were not found sex/gender difference in FSIQ (Banach et al., 2009). To conclude, females with ASD have significantly lower FSIQ than males with ASD ($p<.001$). See also Figure 7 in which a meta-analysis is presented. The meta-analysis includes all studies that investigated sex/gender differences in FSIQ among ASD.

In the context of NVIQ and VIQ, two studies found that females have a more balance cognitive profile than males. In these studies, males had bigger discrepancy between NVIQ and VIQ than females with ASD (Frazier et al., 2014; Lehnhardt et al., 2016). Some studies failed to find sex/gender differences in FSIQ (Fulton et al., 2017; Kumazaki et al., 2015; May et al., 2016; Mussey et al., 2017), NVIQ (Bölte et al., 201; Kumazaki et al., 2015; May et al., 2016; Mussey et al., 2017; Reinhart et al., 2015) or VIQ (Ankeman et al., 2014; Kumazaki et al., 2015; May et al., 2016; Mussey et al., 2017; Reinhart et al., 2015). Altogether, there appears to be a tendency that females with ASD have lower FSIQ, NVIQ and VIQ than males with ASD.

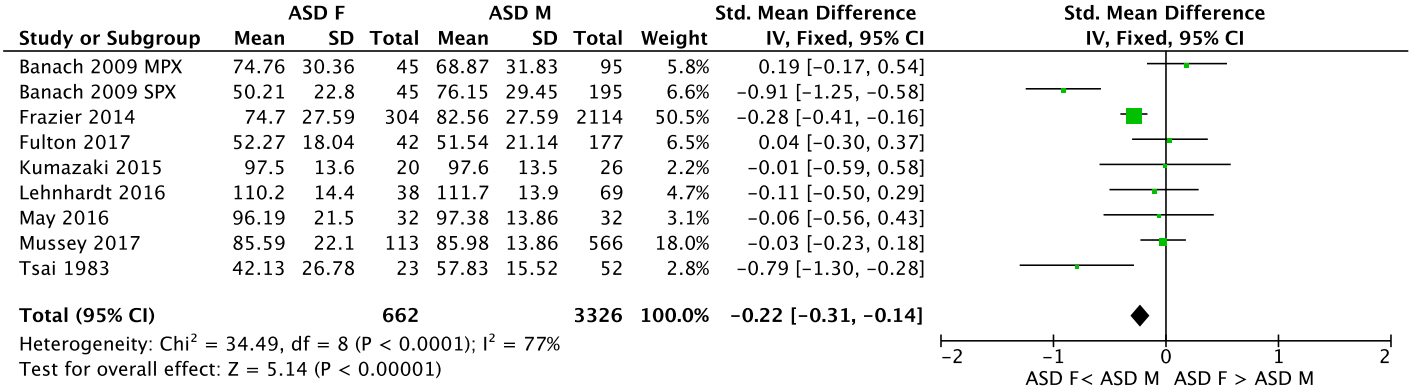

Figure 7. A meta-analysis of studies that investigated sex/gender differences in FSIQ in ASD. Females with ASD have lower FSIQ than males with ASD ($p<.001$).
Abbreviations: MPX=multiplex ASD child families, SPX= simplex ASD child families.

3.2.2. Language

All but one of studies that have included only HFASD participants, reported that females are better in language abilities than males. Studies have shown that females with HFASD are better than males with HFASD in total verbal fluency (Goddard et al., 2014; Lehnhardt et al., 2016), semantic verbal fluency (Schneider et al., 2013), word generation (Lai et al., 2012) and word recognition in multisensory speech processing tasks (Ross et al., 2015). One study with HFASD individuals found mixed results. According to this study, females with HFASD are better than males with HFASD in semantic verbal fluency but poorer in phonemic verbal fluency (Kiep & Speks 2017). Some of these studies also compared language abilities between NTs. Based on the findings reported in these studies, it seems that this difference is not specific to ASD group. Many of the studies in NTs also found that females perform better than males in language tasks (Goddard et al., 2014; Lai et al., 2011; Ross et al., 2015). In summary, 5/6 of studies that investigated language abilities among HFASD reported that females have better language abilities than males. However, the sex/gender differences in verbal functioning among HFASD group may merely reflect the typical sex/gender differences.

Studies that have included both HFASD and LFASD participants have reported inconsistent results. According to some studies, females with ASD have weaker skills than males with ASD at vocabulary (Carter et al., 2007a), non-word repetition (Carter et al., 2007a) and language abilities (Backer van Ommeren et al., 2017; Øien et al., 2018; Reinhardt et al., 2015). Other studies, in turn, found no sex/gender differences in expressive and receptive language skills among ASD children (Carter et al., 2007a; Hartley and Sikora, 2009). One study, including only LFASD individuals suggests that females have weaker receptive language skills than males (Konsantareas et al., 1989). Together the existing evidence suggests that among the HFASD group females perform better than males in tasks that measure verbal fluency which was true also among the NT group. Among those studies that have both HFASD and LFASD participants, results are mixed, but it is possible that females with LFASD have weaker language skills than males with ASD.

3.2.3. Executive functions

Two studies have found that among adults and adolescents with HFASD, females perform worse in a task that measures cognitive flexibility (Kiep & Speks 2017; Memari et al., 2017). In these studies, females with HFASD made more perseverative errors than males with HFASD. However,

one study suggests that females with HFASD perform better than males with HFASD in another task that also measures cognitive flexibility (Bölte et al., 2011). There is also one study that did not find differences between females and males with HFASD is cognitive flexibility (Lehnhart et al., 2016). In the domain of planning abilities, there are also two studies that did not find sex/gender differences (Bölte et al., 2011; Kiep & Speks 2017). In the context of inhibition, one study found that among children with HFASD females performed poorer than males in task that measure inhibition via stopping time (Lemon et al., 2011). Two studies found no sex/gender differences in response inhibition among adults with HFASD (Lai et al., 2012, 2017). Two studies have found that in HFASD, females perform better than males in tasks measuring processing speed (Kumazaki et al., 2015; Lehnhardt et al., 2016) and working memory (Kiep & Speks 2017). In the context of central coherence, one study found that females with HFASD performed better than males with HFASD (Lai et al., 2012) whereas another study did not find sex/gender differences in central coherence among HFASD (Lehnhardt et al., 2016). In the tasks measuring visuospatial abilities, the results are also mixed. One study found that females with HFASD perform worse than males with HFASD (Bölte et al., 2011) whereas another study did not find sex/gender differences (Kumazaki et al., 2015). One study found, that within a group which has both HFASD and LFASD, females have more executive function problems than males (White et al., 2017). There were no studies that compared executive functions between females and males in LFASD. All in all, five studies have found that females with HFASD are better than males with HFASD in some tasks that measure executive function and also five studies have found that males with HFASD are better than females with HFASD in some tasks. Hence, the results concerning sex/gender differences in executive functions are rather inconsistent. Probably the only conclusion that can be drawn is that based on the current evidence there are no clear differences in executive functions between females and males with HFASD. Inconsistent results could also partially relate to problems in categorizing executive tasks. Even within the same executive domain, poor correlations among tasks are often observed, making it difficult to perform a systematic analysis.

3.2.4. Emotion and face recognition

Two studies reported that adult females with HFASD are better than adult males with HFASD in recognizing emotions from faces and from the eyes area only (Lai et al., 2012; Sucksmith et al., 2013). One study suggests that among children with HFASD, females perform worse than males in emotion recognition tests (Rynkiewicz et al., 2016). However, 3 out of 6 studies did not found sex/gender differences in emotion recognition in ASD. There are several studies in adults with

HFASD or ASD with no specified level of functioning that have not found sex/gender differences in recognizing emotions from faces (Schneider et al., 2013), or eyes (Baron-Cohen et al., 2015 Lai et al., 2017; Lehnhardt et al., 2016). One of these studies reported also that among NTs, females perform better in emotion recognition tests, but among ASD typical sex/gender difference are not evident (Baron-Cohen et al., 2015). However, another study reported that in both HFASD and NT groups there was significant sex/gender difference towards females being better in emotion recognition (Sucksmith et al., 2013), thus providing contrasting findings.

There was only one study that has compared face identity recognition between females and males with ASD. This study did not find sex/gender differences in children with ASD (Coffman et al., 2015). No studies investigating sex/gender effects in emotion recognition or face identity recognition in LFASD were found. To conclude, most of the studies did not find differences between females and males with ASD in emotion recognition and there is also no evidence of sex/gender effects in face identity recognition.

3.2.5. Empathizing and systemizing

One study with 811 participants found, that adult females with ASD are better than adult males with ASD at empathizing (Baron-Cohen 2014). Similar findings have also been reported among NT population: Females are better at empathizing, but worse in systemizing (Auyeung et al., 2009; Baron-Cohen et al., 2003b; Baron-Cohen et al., 2014; Park et al., 2012; Schwarz et al., 2011; Wakabayashi et al., 2007). It should be noted, however, that 6 other studies with altogether 640 participants have not found sex/gender differences in empathizing and systematizing among children (Auyeung et al., 2009) or adults with ASD (Baron-Cohen et al., 2003b; Lai et al., 2011; Lehnhardt et al., 2016; Park et al., 2012; Wakabayashi et al., 2007). There is also one study including 45 participants, suggesting that adult males with ASD are better at empathizing than adult females with ASD (Schwarz et al., 2011). However, in this study, females also had significantly higher Autism Quotients than males, indicating that females were more severely autistic than males in this sample (Schwarz et al., 2011). In conclusion, it is possible that among ASD population gender differences in empathizing and systematizing are not as prominent as among NTs.

3.3. Comorbidity

3.3.1. Psychiatric comorbidity

Many psychiatric comorbid problems are found to be more common in females with ASD than in males with ASD (see Table 6). It has been suggested that females with ASD have more depression (Hartley et al., 2009; Oswald et al., 2016; Solomon et al., 2012) and anxiety (Amr et al., 2011; Hartley et al., 2009; Solomon et al., 2012) than males with ASD. There are also studies that have failed to find sex/gender differences in anxiety or depression (Amr et al., 2012; Holtmann et al., 2007; Lai et al., 2011, 2017; Magiati et al., 2016; Pisula et al., 2017; Worley et al., 2011). Age may have some effect on depression symptoms in males and females with ASD. One study found that during early adolescence, females with ASD suffer more from depression than males with ASD, but during late adolescence sex/gender differences were no longer found (Oswald et al., 2016).

Self-injury and self-directed verbal aggression are found to be more common in females with ASD than in males with ASD (Cohen et al., 2010; Frazier et al., 2014). Other studies did not find significant sex/gender differences among children with ASD regarding self-injurious behavior (Baghdali et al., 2003; Duerden et al., 2010). However, in one of these studies (Baghdali et al., 2003), females were slightly overrepresented in the group that had self-injurious behavior. Fifty-eight percent of females were found to have self-injurious behavior, whereas in males this number was 48% (Baghdali et al., 2003).

Phobias are found to be more common in females with ASD than males with ASD. Phobias have been found in 48.8% of the females and 39.1% of the males (Mayes et al., 2013). The most common phobias that have been reported are fear of toilets, elevators, vacuum cleaners, thunderstorms, heights and the worry for dying (Mayes et al., 2013).

One study found that anorexia nervosa is more common among females with ASD than in NT females (Pohl et al., 2014). There were no studies that compared eating-related symptoms between ASD females and males.

Schizophrenia spectrum traits are found to be more common in females with ASD than in males with ASD according to parents reports (Gadow et al., 2012). However, according the teachers reports, no differences between females and males in schizophrenia spectrum traits have been found (Gadow et al., 2012). Another study found that adult females with LFASD have less diagnosed schizophrenia spectrum disorders than adult males with LFASD (Tsakanios et al., 2011).

Some studies found that females with ASD have less hyperactivity and inattention than males with ASD (Mandy et al., 2012; May et al., 2016). In contrast, one study found that

females with ASD have more attention problems than males with ASD (Hotlmann et al., 2007). Most of the studies failed to find sex/gender differences in attention problems (Amr et al., 2011; Hartley et al., 2009; Pisula et al., 2017, Postorino et al., 2015), hyperactivity (Frazier et al., 2014) or ADHD (Amr et al., 2012) among children with ASD.

One study found that among children with ASD females have less delinquent behavior than males (Amr et al., 2011) whereas another study found that among children with ASD females have more irritability and externalizing problems than males (Frazier et al., 2014). One study also found, that in tasks that measure aggression, females with HFASD have less reactive aggression than males with HFASD (Kaartinen et al., 2014). Many studies found no sex/gender differences among children with ASD in conduct behavior (Amr et al., 2012; Worley et al., 2011), challenging behavior (Kozlowski et al., 2012), aggressive behavior (Amr et al., 2012; Hartley et al., 2009; Holtmann et al., 2007; Pisula et al., 2017; Postorino et al., 2015), externalizing problems (Hartley et al., 2009; Pisula et al., 2017; Postorino et al., 2015) or delinquent behavior (Holtmann et al., 2007; Pisula et al., 2017).

In conclusion, the existing body of evidence suggests that females with ASD have overall more psychiatric comorbid problems than males with ASD. Especially it seems, that females with ASD have more depression, anxiety, self-injury, phobias, irritability and lethargy than males with ASD. See Table 6 for the number of studies that have investigated psychiatric and neuropsychiatric problems.

Table 6. The number of studies and participants in studies that have compared psychiatric and neuropsychiatric comorbid diagnosis and symptoms between females and males with ASD.

	ASD Females > ASD Males Studies/participants	ASD Females < ASD Males Studies/participants	ASD Females = ASD Males Studies/participants
ADHD / hyperactivity / inattention	1/46	2/394	5/2807
Aggressive behavior	0/0	1/35	5/435
Anxiety	3/299	0/0	6/501
Conduct disorder /challenging behavior	0/0	0/0	2/227
Delinquent behavior	0/0	1/60	2/116
Depression	4/331	0/0	8/460
Eating problems	0/0	0/0	1/70
Externalization	1/2418	0/0	4/389
Internalization	1/40	0/0	5/2807
Irritability	1/2418	0/0	0/0
Lethargy	1/2418	0/0	0/0
Obsessive compulsive symptoms	0/0	0/0	1/62
Personality disorder	0/0	1/150	0/0
Phobias	1/1033	0/0	0/0
Schizophrenia spectrum traits or disorder	1/119	1/150	0/0
Self-injury / self-directed aggression	2/2684	0/0	2/450
Sleep problems	0/0	1/199	0/0
Social problems	1/46	1/60	1/70
Somatic complains	0/0	0/0	4/375
Thought problems	1/46	0/0	2/130
Withdrawal	1/46	0	3/329
Any psychiatric disorder or problem	19/11944	7/948	51/9228

3.3.2. Neurological comorbidity

ASD is associated with some neurological comorbid problems. Epilepsy and seizures are found to be more common in females with ASD than males with ASD (Ben-Iztchak et al., 2013; Bolton et al., 2011). Epilepsy was found to be diagnosed in 30% of females with ASD and 18% of males with ASD (Bolton et al., 2011). Age at onset of epilepsy was also found to be slightly higher in males with ASD than females with ASD, but the difference was not significant (Bolton et al., 2011). It is also reported that epilepsy is more treatment-resistant in females with ASD than males with ASD (Blackmon et al., 2016).

Some studies have found that macrocephaly is equally common in females and males with ASD (Ben-Itzchak et al., 2013; Lainhart et al., 1997). There is also a study reporting that macrocephaly is more common in males with ASD than in NT males, but they failed to find difference in macrocephaly prevalence between females with and without ASD (Campdell et al., 2014). According to one study, microcephaly is more common among females with ASD than males with ASD. Microcephaly was found in 15.1% of females with ASD whereas microcephaly was presented 4.5% of males with ASD (Ben-Itzchak et al., 2013).

Mild non-specific neuroimaging abnormalities (Blackmon et al., 2016) and minor neurological deficits (Ben-Itzhak et al., 2013) are found to be more common in females with ASD than in males with ASD. The most common minor neurological deficits are found to be hypotonia, hyperflaxity of joints, abnormal tendon reflexes, hypertonia, and cerebellar dysfunction (Ben-Itzchak et al., 2013). It is suggested, that higher rates of epilepsy and minor neurological deficits reflect a greater neurologic burden in females with ASD as compared to males with ASD (Blackmon et al., 2016).

3.4. Neurobiology

3.4.1. Brain structure and functioning

Most of the studies that investigated sex/gender differences in brain anatomy or functioning in ASD found some differences between females and males (see Figure 8). Differences are found especially in brain areas involved in social communication and interaction. In these studies, alterations in brain structure have been measured with magnetic resonance imaging (MRI).

Enlargement of the brain is found both in females with ASD and males with ASD (Bloss et al., 2007; Piven et al., 1996; Schumann et al., 2009, 2010). Abnormally high growth is found in different brain areas in both females and males with ASD (Beacher et al., 2012a; Bloss et al., 2007; Lai et al., 2013; Retico et al., 2016; Sparks et al., 2002; Supekar et al., 2015). There is also evidence of a correlation between and sex/gender, brain abnormalities, and some ASD symptoms. Structural differences in the gray matter of the motor cortex and supplementary motor area have been found to be correlated with severity of RRBIs in females, whereas structural differences in gray matter in the right putamen are correlated with severity of RRBI in males (Supekar et al., 2015). Enlargement of gray matter volumes in the anterior cingulate cortex was found to be specific only to ASD females (Retico et al., 2016). These areas are involved in affective processing and generally thought to contribute to social and cognitive disturbances that are typical for ASD (Retico et al., 2016). Males with ASD are found to have specific enlargement of superior frontal gyrus volume, which is suggested to be involved in social perception and theory of mind (Retico et al., 2016). In some reports females with ASD have been found to have reduced gray matter in the right limbic region, which further correlates negatively with social communication abilities (Craig et al., 2007). Amygdala volume is shown to be enlarged both in females and males with ASD but enlarged gray matter volumes correlated with social deficits only in males (Schumann et al., 2009). Some studies found amygdala enlargement only in males with ASD

(Sparks et al., 2002; Supekar et al., 2015), but this was not correlated with social deficits (Supekar et al., 2015). Finally, in one study, reduction of gyrification in the ventromedial prefrontal cortex and orbitofrontal cortex was found only in ASD males (Schaer et al., 2015). These brain areas are associated with social abilities (Schaer et al., 2015).

Many studies have found atypical sexual dimorphism of the brain in ASD. Normal neuroanatomical sex/gender differences are attenuated among ASD participants (Beacher et al., 2012a; Retico et al., 2016). In NT participants females have smaller gray matter volume than males, whereas in ASD participants there are no differences between females and males because gray matter volume is reduced in ASD males (Beacher et al., 2012a). One study, that probabilistically predicted the assigned sex of participants based on neuroanatomy, found that ASD females, when compared to NT females, demonstrate significantly often a male neuroanatomical brain phenotype (Ecker et al., 2017). This study found also that females with ASD also have greater abnormalities in cortical neuroanatomy than males with ASD (Ecker et al., 2017). It should be noted, however, that in this study female participants had more severe ASD symptoms than males. Another study found neuroanatomical abnormalities in areas that are sexually dimorphic within normal population in females with ASD but not in males with ASD (Lai et al., 2013).

Task-related brain activation has been measured with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). One study measured brain activation during mental rotation and verbal fluency. During verbal fluency tasks, the study did not find differences in task performance between ASD and NTs, but when compared with NTs, ASD participants had greater activity in the left occipitoparietal and inferior prefrontal cortex (Beacher et al., 2012b). In the mental rotation task there was a significant sex-by-diagnosis interaction. Moreover, greater activation in the occipital, temporal parietal and middle frontal regions was found in ASD males than ASD females (Beacher et al., 2012b). In contrast, among the NT group there was found greater activation in these brain areas in females rather than males (Beacher et al., 2012b). Authors suggested, that greater activation in ASD males and NT females can reflect a less efficient strategy for task solving that relies more on local processing than global processing (Beacher et al., 2012b).

Three studies have measured brain activity during tasks that are related to social communication and interaction. During empathy task, the activation of the amygdala, that is involved in emotional and social processing, was found to be significantly decreased in ASD females compared to that of NT females, whereas ASD males did not differ from NT males (Scheider et al., 2013). On the other hand, males with ASD had atypical increased activation in the medial frontal gyrus during empathy task that was not seen in females with ASD or NT males and females (Scheider et al., 2013). The medial frontal gyrus is involved in processing of theory of

mind, and authors suggested that hyperactivation of this area can reflect compensatory mechanisms because of initial problems of theory of mind (Scheider et al., 2013). The authors also suggested that " the affective parts of the brain" could be more impaired in females with ASD, whereas males with ASD might have more severe impairments in brain areas more closely involved in cognitive functions (Scheider et al., 2013). Another study found, that during theory of mind -task ASD males had decreased activity in the posterior superior temporal sulcus, compared to ASD females and NT participants (Kirkovski et al., 2016). The superior temporal sulcus is involved in social cognition and understanding the meaning of motions and actions (Kirkovski et al., 2016). One study has reported that females with ASD have more atypical brain responses to faces than males with ASD (Coffamn et al., 2015). At a neural level, females with ASD showed attenuate neural response to faces (Coffamn et al., 2015). The deficits in face processing in females with ASD was found to correlate also with severity of social communication and behavioral problems and overall symptom severity (Coffman et al., 2015). Authors suggested, that the differences between females and males with ASD in neural responses to faces could be due to the role of sex/gender in the way we remember images, or due to differences in point of gaze (Coffman et al., 2015).

To conclude, there are sex/gender differences in ASD in brain areas that are involved in social and emotional processing and also motor areas that are connected RRBI. There are also sex/gender differences in ASD in the brain activity during tasks that require visuospatial processing, emotion processing, social cognition and face processing.

Figure 8. The brain areas in which the structure or functioning differs in ASD females from other studied groups (ASD males, NT females, NT males) are illustrated in pink in this picture. There are alterations in many areas that are involved in social processing. The picture is combined from articles that have used MRI or fMRI and have provided brain coordinates (Alaerts et al., 2016; Beacher et al., 2012a, 2012b; Ecker et al., 2017; Craig et al., 2007; Kirkovski et al., 2016; Lai et al., 2013; Retico et al., 2016; Scheinder et al., 2013; Supekar et al., 2015). The picture is created with BrainMap (Fox & Lancaster 2002).

3.4.2. Brain connectivity

Many studies found brain hypoconnectivity in ASD. Atypical hypoconnectivity has been reported in HFASD males but not HFASD females. HFASD males have hypoconnectivity in frontal tracts (Zeestrarten et al., 2017) and in the corpus callosum, cingulum and corona radiate (Beacher et al., (2012a), whereas there were no differences in the connectivity of these areas in HFASD females and NT females (Beacher et al., 2012a; Zeestraten et al., 2017). Another study found functional hypoconnectivity in HFASD males and functional hyperconnectivity in HFASD females (Alaerts et al., 2016). Finally, one study failed to find any sex/gender differences or any other differences in brain connectivity between HFASD and NT participants (Kirkovski et al., 2015).

Among studies in LFASD, one study found hypoconnectivity both in females and males, but in different brain areas. In LFASD females hypoconnectivity was observed in the anterior frontal cortex, superior frontal cortex and posterior parietal cortex (Nordahl et al., 2015). LFASD males also have hypoconnectivity in the orbitofrontal cortex and trend level hypoconnectivity in the superior frontal cortex (Nordahl et al., 2015). LFASD males also have hyperconnectivity in the anterior frontal cortex (Nordahl et al., 2015). There was also increased mean, axial and radial diffusivity in females with LFASD when compared to NT females. LFASD males, in turn, did not differ from NT males (Nordahl et al., 2015). When viewed together, most of the studies have found hypoconnectivity in both LFASD as well as HFASD males. Among studies in ASD females, the results have not been consistent.

3.5. Neurogenetics

3.5.1. Genetic burden

According to a twin study, heritability is .87 for females and .73 for males (Taniai et al., 2008). Recurrence rates of ASD diagnosis in siblings are also higher when affected individuals are females rather than males (Palmer et al., 2017). When the affected child is female, the sibling recurrence rate is 7.6% for female siblings and 16.7% for male siblings. When the affected child is male, the sibling recurrence rate is 4.2% for female siblings and 12.9% for male siblings. To conclude, heritability estimates in ASD are higher for females than males.

Females with ASD also have higher proportions of de novo mutations, more deletions and an increase in large copy number variants (CNVs) compared to males with ASD (Jacquemont et al., 2014; Levy et al., 2011). These results may reflect a higher genetic load in females with ASD than

that of males with ASD (Jacquemont et al., 2014; Levy et al., 2011; Palmer et al., 2017; Taniai et al., 2008). These findings together suggest that females must have a higher genetic burden than males to fill the diagnostic criteria of ASD.

3.5.2. X-chromosome

Differences of X chromosome inactivation between ASD females and NT females has been investigated in three studies. One study revealed increased skewness of X-chromosome in females with ASD as compared to NT females (Talebizadeh et al., 2005). Highly skewed X-chromosome inactivation was found in 33% of the females with ASD and in 11% of NT females (Talebizadeh et al., 2005). Also the mothers of ASD children have unusually skewed X-chromosome (Talebizadeh et al., 2005). Another study failed to find any significant increase in skewness in ASD females. However, a linkage in the X-chromosome associated with ASD was found among subgroups who had high skewness of the X-chromosome (Gong et al., 2008). One study searched for single nucleotide polymorphisms (SNPs) from the X-chromosome that are inactivated in NT females but not in ASD females, but they did not find such (Gockley et al., 2015). In conclusion, in some cases the unusual skewness of X-chromosome can be linked with ASD, but in many cases differences in X-chromosome inactivation between NT and ASD females were not found.

3.5.3. Association and linkage studies

Genetic association and linkage studies have identified many sex/gender specific gene associations to ASD and genes that increase the liability to ASD specifically for only females or males. Many sex/gender-specific ASD associations and linkages appear in X chromosome (see Figure 9). Female-specific linkages have been found at chromosome 4 and Xq27-Xq28 (Gong et al., 2008; Schellenberg et al., 2006). Male-specific linkages, in turn, have been found on 1p31.3, 5q12.3, 9q33.3, 11, 13q33.3, 16p, 17q11-17q21 and Xp22.33/Yp11.31 (Cantor et al., 2005; Chang et al., 2013; Lamb et al.,2005; Schellenberg et al., 2006; Stone et al., 2004; Szatmari et al., 2007; Werling et al., 2014).

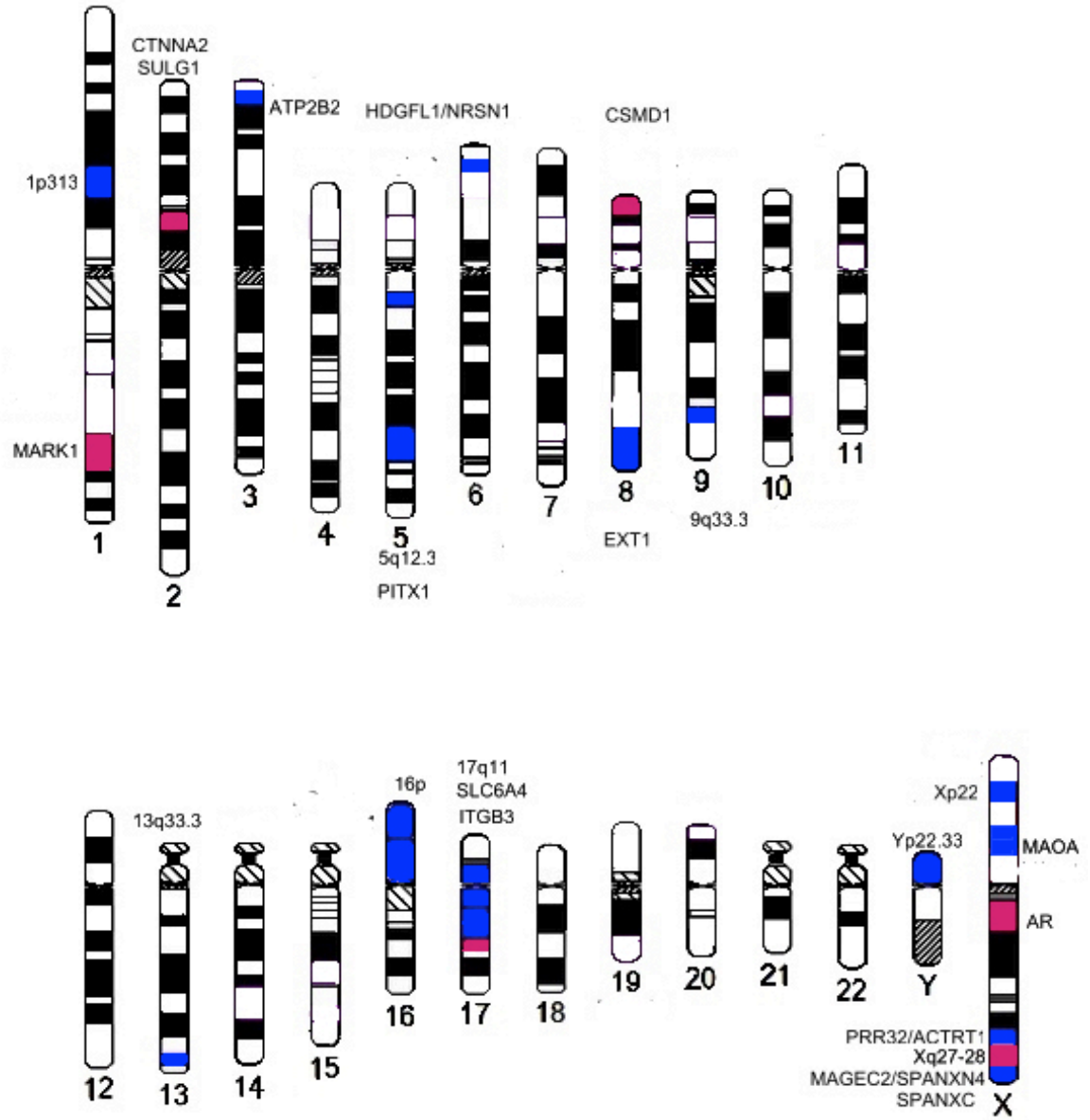

Figure 9. Sex/gender related chromosomes and genes that are associated with ASD. Pink color refers to female only association and blue color to male only associations. Especially in the X-chromosome there are many genes that are associated with ASD. The picture of chromosomes was drawn with CyDas (Hiller et al., 2004).

Many genes involved in brain development and functioning are associated with ASD. Female-specific associations have been found in the genes encoding *ITGB3, MARK1*, and *CTNNA2* (Carayol et al., 2011; Mitra et al., 2016). In one study, *NLGN4X* was associated with ASD only in females (Chakrabarti et al., 2009), but there is another study in which it linked to ASD both in females and males (Mitra et al., 2016). *ITGB3* is participates to cell signaling, *MARK1* regulates neuronal migration, *NLGN4X* is involved in synapse formation and maintenance of the central nervous system and *CTNNA2* is involved in cell-cell adhesion and differentiation in the nervous system and synaptic plasticity (Carayol et al., 2011; Chakrabarti et al., 2009; Mitra et al., 2016). Male-specific effects in ASD have been found in the genetic association of markers for *ATP2B2, NLGN3, PITX1, SLC6A4*, *NRSN1* and *MAOA* (Carayol et al., 2011; Schuch et al., 2016; Verma et

al., 2014; Yu et al., 2011). *ATP2B2* affects intracellular calcium homeostasis that in turn affects cell signaling, *NLGN3* is involved in formation and plasticity of synapses, *PITX1* affects brain development, *SLC6A4* regulates serotonin transmission, and *NRSN1* is implicated in brain development and *MAOA* is involved in metabolism of dopamine, norepinephrine and serotonin (Carayol et al., 2011; Schuch et al., 2016; Verma et al., 2014; Yu et al., 2011). Both female and male associations are found with *CNTNAP2, JARID2, EN2, ARNT2* and *HOXA1* that are involved in brain development (Carayol et al., 2011; Chakrabarti et al., 2009; Mitra et al., 2016). *HOXA1* is also associated with head size and head growth rate (Carayol et al., 2011). Both female and male associations are also found with *NTRK1* that is involved in the development of the sensory system (Chakrabarti et al., 2009).

Many genes that are involved in sexual differentiation and the production of steroid hormones are associated with ASD. Genes *CYP11B1, CYP17A1, CYP19A1* are associated with both females and males with ASD (Chakrabarti et al., 2009). These genes are involved in the synthesis of steroid hormones, and they also affect the development of sexual dimorphism (Chakrabarti et al., 2009). Additionally, the expression of the RORA protein, that regulates *CYP19A1*, differs between females and males in the frontal cortex (Hu et al., 2015). One study found female-specific association of the *AR* gene with ASD (Henningsson et al., 2009). *AR* encodes testosterone receptors, and it could affect prenatal exposure to androgens (Henningsson et al., 2009). It has been suggested that excessive exposure to androgens during prenatal period is one possible etiological factor for ASD. There is also both female and male association with *ESR2* that encodes estrogen receptors (Chakrabarti et al., 2009). Estrogen affects neuronal development in the fetal brain via these receptors and mediates social interaction via its receptors in the hippocampus and the amygdala (Chakrabarti et al., 2009).

Many genes that are involved in social and emotional behavior are also associated with ASD. Both female and male associations have been found with *OXT, OXTR* and *AVPR1B* (Chakrabarti et al., 2009). *OXT* and *OXTR* encodes oxytocin receptors, and *AVPR1B* encodes vasopressin receptors (Chakrabarti et al., 2009). Both oxytocin and vasopressin affect social communication and behavior. There is also both female and male association with *WFS1* that is expressed in the amygdala that is involved in fear-related processes (Chakrabarti et al., 2009). Two SNPs of *WFS1* are also shown to correlate with scores of Autisms Quotient and Empathy Quotient (Chakrabarti et al., 2009). Additionally, one study found female specific association of *MAOB* that is also involved in metabolism of dopamine, norepinephrine and serotonin and affects to social cognition (Chakrabarti et al., 2009). Another study found association with both females and males but only males' symptom severity and serotonin levels correlate with *MAOB* association

(Chakraborti et al., 2016). Among females, no correlation between symptoms severity and *MAOB* association was found. In conclusion some differences in the genetic liability of ASD between females and males clearly exists. In the future, it is important to conduct more linkage and association analyses separately for females and males.

One study found, that there are several SNPs that are associated with antropometric heterogenous traits in females and males with ASD (Mitra et al., 2016). Antropometric heterogenous traits are for example BMI, height, weight, and waist and hip ratio. This finding lead researchers to hypothesize, that there is pleiotropy between secondary sex characteristics and ASD and therefore the gender bias of ASD is based on the same biological mechanisms that affect sexual dimorphism in general (Mitra et al., 2016). In summary, females and males seems to have at least partially different susceptibility genes for ASD.

3.6. Neuroendocrinology

3.6.1. Testosterone

Females with ASD have a higher serum testosterone level (Bejerot et al., 2012; Geier & Geier 2007) and a higher free androgen index (Schwarz et al., 2011; Steeb et al., 2014) than NT females. Free androgen index is calculated by dividing total testosterone level into the sex-hormone binding globulin. Females with ASD have more often masculinized facial features and voice and more often sex-steroid related problems, like hirsutism, severe acne, an irregular menstrual cycle and dysmenorrhea than NT females (Ingudomnukul et al., 2007; Pohl et al., 2014). Females with ASD are also more often bisexual, asexual and transgender than NT females (Ingudomnukul et al., 2007; Pohl et al., 2014).

Effects of testosterone is also studied indirectly by investigating androgynous features. Bejerot et al., (2012) found, that both females and males with ASD have more androgynous physical features than their NT counterparts. Males with ASD, compared to NT males, have a significantly more feminine body, face features, voice and digit ratio, that is associated with fetal testosterone levels, whereas females with ASD have significantly more masculinize face features and voice than NT females (Bejerot et al., 2012). Furthermore, the androgynous facial traits correlate positively with ASD traits in both females and males. (Bejerot et al., 2012). In conclusion, there appears to be correlation between testosterone related problems and testosterone levels with ASD.

3.6.2. Oxytocin and vasopressin

Both ASD and NT females have higher oxytocin levels and lower vasopressin levels than ASD and NT males (Miller et al., 2013). That is, there is no evidence of sex/gender differences in oxytocin or vasopressin levels of ASD. However, correlations between oxytocin and vasopressin levels and ASD symptoms are found (Miller et al., 2013). A significant correlation between oxytocin level and central coherence has been reported across the female population (Miller et al., 2013). In ASD females, there was additionally a trend towards correlation between oxytocin level and RRBIs (Miller et al., 2013). Among males with ASD, oxytocin levels have not been found to correlate with any ASD symptoms (Miller et al., 2013). Higher vasopressin levels significantly correlates with self-injurious behavior and overall RRBIs among ASD females (Miller et al., 2013). Trend level correlations between vasopressin level and compulsive and ritualistic behavior have also been found among ASD females (Miller et al., 2013). Among ASD males, significant association between vasopressin level and social cognition/motivation has been found (Miller et al., 2013). Additionally, lower vasopressin levels are shown to be associated with trend level of self-injurious behavior and restricted interests (Miller et al., 2013). In conclusion, there were no overall differences between ASD and NT groups in oxytocin and vasopressin serum levels. However, sex/gender differences were found in the correlations between ASD symptoms and oxytocin and vasopressin serum levels.

4. Discussion and conclusions

This systematic review about autism in females covers the following areas of ASD: symptomatology, neuropsychology, comorbidity, neurobiology, genetics and neuroendocrinology. This is the first review to provide such a wide picture of sex/gender differences in ASD. The purpose of this review was to find 1) is there evidence of sex/gender differences in ASD symptoms and comorbid disorders, 2) is there evidence of sex/gender differences in ASD etiology, and 3) what kind of support different explanations and theories get from the existing body of evidence. Purpose was also to integrate the existing theories into one model that takes account to different aspects of sex/gender differences in ASD. In following paragraphs, the results and significance of this review will be discussed. Possible limitations and future study directions are discussed as well.

4.1. Underdiagnosing of ASD in females

The proposed underdiagnosing of females with HFASD gets support from many research areas. The most evident related finding of this was that, as expected, the clinical features of HFASD females differ partially from clinical features of HFASD males (See Table 7). Sex/gender differences in symptoms are suggested to be the reason for missed diagnoses in females with ASD, since the criteria of ASD and also the screening instruments of ASD are developed according to typical symptoms of ASD in males (Haney 2016).

Sex/gender differences were found in the following areas of ASD symptoms: 1) problems of social communication and interaction, 2) restrictive and repetitive behavior and interests, 3) sensory symptoms. Females with HFASD have less problems in social communication and interaction than males with HFASD (see Figure 3). Females with HFASD are also found to have better camouflaging skills when compared to males with HFASD, meaning that they mask their social deficits (Lai et al., 2017; Ormond et al., 2018). However, the continuous efforts to act like NTs can require cognitive resources that may lead to increased fatigue and anxiety (Livingston et al., 2018). This is in line with the findings about psychiatric comorbid problems, since it is shown that females with HFASD suffer more from anxiety, depression and self-injury than males with ASD (see Table 6). Many neuroimaging studies have also found sex/gender differences in ASD in brain areas involved in social communication and interaction (see Figure 8).

Another important sex/gender difference in the symptoms of ASD was found in RRBIs. As expected, females with HFASD are found to have fewer RRBIs than males with HFASD (see Table 4). There are several possible explanations for this. It is possible, that RRBIs are not noticed in females as they may be qualitatively different from RRBIs in males (note that RRBIs were originally described according to typical symptoms in males). The restricted interests observed in females are more socially accepted (e.g. collecting stamps, rocks, or stickers), while in males with ASD it is more typical that RRBIs are fixated, stereotyped and narrow (e.g. lining up cars and fascination for parts of objects) (Duvekot et al., 2017; Hiller et al., 2014). It is also possible, that sex/gender differences in RRBIs are related to sex/gender differences in neuroanatomy. One study found neuroanatomical sex/gender differences in ASD in motor areas that are generally considered to be involved in RRBI, and these differences also correlated with the severity RRBIs (Supekar et al 2015). Also the levels of vasopressin and oxytocin correlate in a different way with RRBI in ASD females and males (Miller et al., 2013). Due to the sex/gender differences in these hormones, it is possible that neuroendocrinological aspects underlie sex/gender differences in RRBI in ASD.

Additionally, females with HFASD are found to have more sensory symptoms than males with HFASD. However, there are only few studies that have measured sex/gender differences in sensory symptoms and all these studies used different questionnaires, so these results should be considered preliminary. To conclude, sex/gender differences could well lead to underdiagnosing in females. This may further cause anxiety and stress, since the females that do not receive the diagnosis despite of their problems are unlikely to get the support that they need.

Females with LFASD differ from males with LFASD in symptoms and associated features (See Table 7 and Figure 4). Females with LFASD are found to have more problems in social communication and interaction and they are also found to have worse language skills than males with LFASD. Sex/gender differences are not found in RRBIs among LFASD. Among both HFASD and LFASD females are found to have lower cognitive ability than males. To conclude, clinical presentation of ASD in females is partially different than ASD in males and this can cause underdiagnosing of females with ASD.

Table 7. The clinical features of ASD in females.

Symptom	HFASD females compared to HFASD males	LFASD females compared to LFASD males
Social interaction and communication	Less problem in social communication and interaction, more camouflaging	More problems in social communication and interaction
Repetitive and restricted behavior and interest	Less RRBIs	No differences
Sensory symptoms	More sensory symptoms	No information
Cognitive ability	Lower cognitive ability	Lower cognitive ability
Language	Better verbal fluency	May have worse language abilities
Executive functions	No clear differences	No information
Empathizing-systemizing	No differences	No information
Psychiatric comorbidity	More unusual fears, self-injury, self-directed verbal aggression	More unusual fears
Neurological comorbidity	More epilepsy and minor neurological dysfunction	More epilepsy and minor neurological dysfunction

Underdiagnosing of females has got support in many areas and it clearly affects negatively both individuals with ASD and scientific studies about ASD. However, even if females are underdiagnosed, there seems to be also a real sex/gender bias in the number of individuals with ASD. It is suggested that there must be etiological causes that underlie this sex/gender bias, and this has led to many theories that try to explain the etiology of the sex/gender bias. Like expected, many sex/gender differences in ASD etiology were found (see Table 8). Also, like expected, all theories and explanations about sex/gender bias got support from more than one research area (see Table 9). In the next chapter, these theories and their connections to etiology and features of ASD are discussed.

4.2. Etiology of ASD in females

Extreme male brain theory and gender deviant theory are both based on the idea that sex/gender bias in ASD is caused by atypical sexual differentiation during gestation. Extreme male brain theory postulates, that ASD is caused by an excessive exposure to testosterone during gestation. Moreover, according to this theory, ASD is more common in males because male fetuses produce normally more testosterone than female fetuses. Extreme male brain theory is supported indirectly by notions that females with ASD are found to have higher testosterone levels than female NTs and also display more testosterone-related problems than NT females (Bejerot et al., 2012; Geier et al., 2007; Ingudomnukul et al., 2007; Pohl et al., 2014). However, no studies investigating the relationship between sex/gender difference and prenatal testosterone level in ASD were found, but there are studies of disorders with an excessive amount of testosterone during fetal development (e.g. congenital adrenal hyperplasia and polycystic ovary syndrome). Females with these conditions were found to have more ASD traits than healthy females, but still most of them do not have ASD (Cherskov et al., 2018; Knickmeyer et al., 2006). Therefore, the excessive exposure to testosterone during gestation appears not be sufficient to cause ASD. Gender deviant theory in turn, got support from the observations of abnormal gender coherence in facial features, voice and neuroanatomy (Bejerot et al., 2012; Ecker et al., 2017). Also, genes *CYP11B1, CYP17A1, CYP19A1, AR* and *ESR2,* which are involved in development of sexual dimorphic characters are shown to be associated with ASD (Chakrabarti et al., 2009; Henningson et al., 2009). There is also evidence of pleiotropy between ASD and sexually dimorphic characteristics (Mitra et al., 2016). Hence, some support was found both for the extreme male brain theory and the gender deviant theory.

The theory of female protective effect has a different point of view. This theory is supported by genetic studies noticing that females have greater mutational burden as well as higher heritability and recurrence rates than males (Palmer et al., 2017; Taniai et al., 2008). Female protective effect has been suggested to be explained by the protective effects of two X-chromosomes. Since females have two copies of X-chromosomes, if there is X chromosomal mutation in one allele, there is the other X-chromosome that has an intact allele. This is supported by findings that many sex/gender specific susceptibility genes are located in the X-chromosome (See Figure 9). Female protective effect is also suggested to result in more severe comorbid problems in affected females than males, and only those, who had great etiological loading reached to the threshold of ASD diagnosis. The notions that females with ASD have lower FSIQ and more frequently some comorbid neurologic problems than males with ASD can reflect this phenomenon. However, there are no studies that would directly show the cause of female protective effect.

Furthermore, a very recent review also suggests, that instead of the female protective effect there could be male vulnerability effect or combined multifactorial effect, meaning that females are protected, and males are vulnerable to ASD (Ferri et al., 2018). To conclude, all theories are capable of explaining some aspects of ASD (see Table 8 and Table 9) but none of them can fully cover the evidence concerning the effect of sex/gender to liability of ASD. What combines these theories is that each of them suggests that some kind of biological factors underlie the sex/gender bias of ASD. These factors are related to biological sex differences and they have mediating effect in ASD.

Table 8. Etiological findings about sex/gender differences in ASD.

		Possible causes of sex/gender bias and/or differences in ASD
Neurobiology	Brain structure	Sex/gender differences in abnormalities of brain areas, abnormal gender coherence.
	Brain functioning	Partially different brain areas activate in females with ASD and males with ASD when they perform specific tasks.
	Brain connectivity	Most of studies have found hypoconnectivity in males. In female the results are heterogenous.
Genetics	Mutational burden	Females with ASD have more de novo CNVs than males with ASD. Heritability estimates are higher for females with ASD than males with ASD.
	X-chromosome	Some females with ASD have skewed inactivation of X-chromosome.
	Association and linkage studies	Some genes and linkages are associated with only females with ASD or males with ASD. It is possible that females and males have partially different susceptibility genes.
Endocrinology	Testosterone	Testosterone levels are higher in males than females and this can be involved in development of ASD. Females with ASD have higher testosterone levels than NT females and more testosterone-related problems.
	Oxytocin and vasopressin	There are sex/gender difference in levels of oxytocin and vasopressin. Different ASD symptoms correlate with levels of oxytocin and vasopressin in females and males.

Table 9. Theories about the cause of male bias in ASD.

Name of theory	Meaning of theory	Evidences for theory
Extreme male brain theory	ASD is a version of "extreme male brain" and therefore there is more males than females who have ASD.	ASD individuals are better at systemizing and poorer at empathizing than neurotypical individuals and this reflect the "extreme male" cognitive style. Females with ASD have higher testosterone levels than NT female and also more testosterone-related problems.
Gender deviant disorder	There are overall deficits in sexual differentiation in ASD.	Androgynous facial features both in females and males with ASD that correlate with ASD traits. Atypical gender coherence in neuroanatomy. Many genes that are involved in sexual differentiation and production of steroid hormones are associated with ASD. Transgenderism is more common in ASD individuals than in general population.
Female protective effect	Females are protected from ASD, so they have in a higher threshold to it. When females have ASD, they usually have greater etiological load than males and therefore more severe problems.	ASD is more common in males than females. Larger CNVs and more de novo mutations in females than males with ASD. For females with ASD there is a higher heritability and recurrence rate than males with ASD. Females are more severely affected than males. Female-male ratio discrepancy is smaller among low function ASD than high function ASD. Epilepsy and minor neurological dysfunctions are more common in females than males with ASD.
Underdiagnoses of females with ASD	The sex/gender bias is not as big as previously thought. Instead there are females with ASD that haven't got proper diagnosis.	Females with ASD are good at camouflaging, coping and masking their social deficits. Females have less RRBIs that can make difficult to recognize them. Population based studies have found that female-male discrepancy is not as big as it has been previously thought.

The purpose of the study was also to integrate the existing theories into one model. Since the existing explanations and theories regarding ASD in females all provide a different point of view to sex/gender bias and none of them can fully explain the bias by itself, it is worthwhile to create a model that provides a wider picture of the bias. Figure 10 illustrates an integrative model summarizing the findings of the present study. In this model there are shown that specific sex/gender differences in susceptibility genes, hormone levels and neurobiology together cause males to be more liable to ASD than females. This in turn has led to biased research that is also related to overall sex/gender bias seen in medical and neuroscience research. Many studies have included only males as participants, even many studies investigating diseases that are as common in

females as in males (Verdonk et al., 2009). Since ASD is much more common in males than females, this general sex/gender bias might have affected ASD research more strongly because there really are more males than females who have ASD. Bias in research, in turn, has led to a biased picture of ASD features since there are sex/gender differences and almost only males with ASD have been as participants in studies. This causes underdiagnosing of ASD females, which has consequences in clinical work. Among clinicians, who make ASD diagnoses, there can be confirmation bias due to the way of thinking that females with ASD are rare. Underdiagnosing of females with HFASD can also have effects on the validity of studies. Most of studies have participants that already have ASD diagnosis and if there are females whose symptoms have not been detected, they are not included in these studies. Usually those who do not have a correct diagnosis are HFASD females. Therefore, females that are included in studies may be generally more affected since they have gotten a proper diagnosis. This is supported by studies that found, that females with ASD have lower FSIQ than males with ASD and also that among LFASD females have more ASD symptoms. Underdiagnosing can cause bias also to genetic studies since only those who are severely affected get diagnosed. In this case, those females who have a diagnosis also have a greater etiological burden. Furthermore, underdiagnosing causes a lack of knowledge of ASD in females and could possibly lead to further attenuation of the sex/gender bias of ASD in future. In future scientific studies, it is very important to analyze females and males with ASD separately to get more information about ASD in females. Also, it would important to conduct studies in representative populations to find undiagnosed females for study participants.

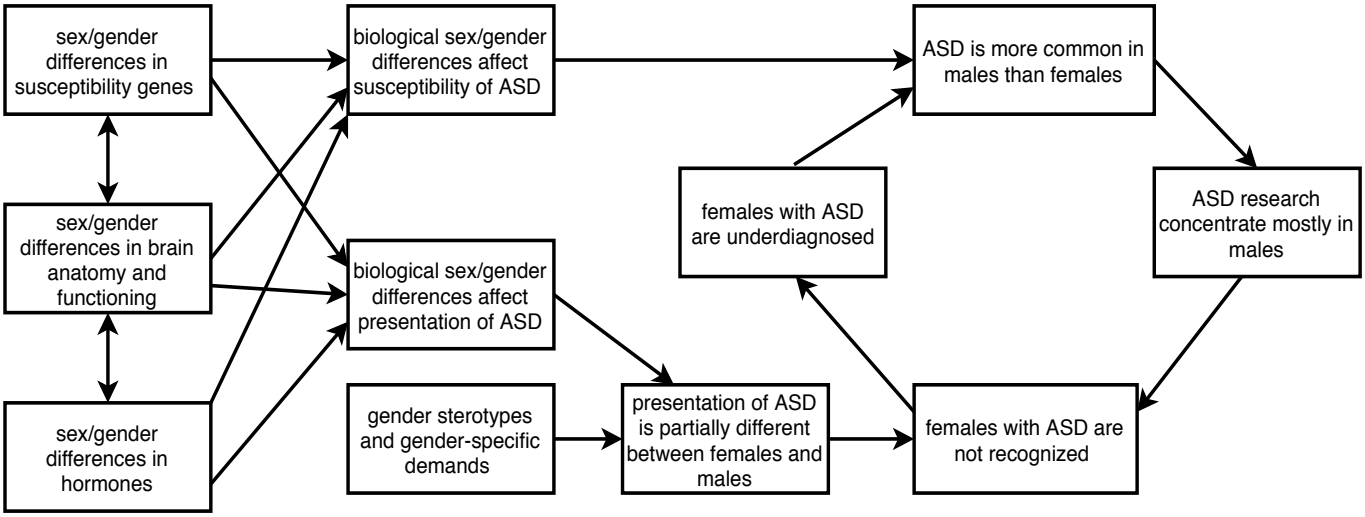

Figure 10. A combined model about sex/gender bias in ASD.

4.3. Limitations and biases of the present study

Main biases of the present study include the following: Only studies that were published in English were included, and it is also possible that some studies were not found when conducting the search. There can also be publication and reporting bias. Studies that found no sex/gender differences among ASD participants may not be published as often as those that do find sex/gender differences. It is also possible that in some of the published studies that have included both females and males as participants did not report gender/sex effects if no differences were found. One possible limitation is also the effect of underdiagnosing of females, like it was discussed earlier in this section. In individual studies, the main limitation is that in many studies the amount of ASD females is quite low when compared to the number of male participants with ASD. A low number of females with ADS affects the validity and reliability of the results. Comorbid diagnoses, that are common in ASD, can also have effects on results. Also, none of the studies reported, how the participants' sex/gender was measured. Variations of gender are much more common among ASD than NTs (Strang et al., 2014), and it is known that transgender individuals have different neuroanatomy than cisgender individuals (Simon et al., 2013). It is possible that these inaccuracies in defining sex/gender caused bias in some studies. In future, it is important to take into account that even a biological sex is not binary category. Some studies also did not report whether the participants are low or high functioning. Since there are some differences between these two groups, the absence of this information can affect the reliability of the results. Also, some studies did not match participants according to the severity of ASD or IQ and so it is possible that differences in these underlie observed sex/gender differences. There are also only few articles about some specific topic and the conclusions are based on a quite small data.

4.4. Conclusions

Despite these limitations, there were also many results that are consistent across many studies and provided valuable knowledge of ASD in females. The most important finding of this study was the wide support of the underdiagnosing of females with HFASD. In clinical work, it is crucial to understand sex/gender differences in ASD and keep in mind that ASD may not be so rare in females tas has been previously thought. Underdiagnosing can have many unfavorable consequences for females with HFASD since if they do not have a diagnosis, they do not get support. HFASD females have been missed both in the diagnosing process and in scientific research for far too long, and it is crucial to pay attention to the existence of this subgroup of ASD in the future.

References

Ainsworth, C., 2015. Sex redefined. Nature 518, 288-291.

Alaerts, K., Swinnen, S.P., Wenderoth, N., 2016. Sex differences in autism: A resting-state fMRI investigation of functional brain connectivity in males and females. Soc. Cogn. Affect. Neurosci. 11, 1002–1016.

American Psychiatric Association, 2000. Diagnostic and statistical manual of mental disorders: DSM-4, fourth ed., text rev. Washington, DC.

American Psychiatric Association, 2013. The Diagnostic and Statistical Manual of Mental Disorders: DSM-5, fifth ed. American Psychiatric Association, Washington D.C.

Amiet, C., GourfinkelAn, I., Bouzamondo, A., Tordjman, S., Baulac, M., Lechat, P., Mottron, L., Cohen, D., 2008. Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. Biol. Psychiatry 64, 577–582.

Amiet, C., Gourfinkel-An, I., Bouzamondo, A., Tordjman, S., Baulac, M., Lechat, P., Mottron, L., Cohen, D., 2008. Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. Biol. Psychiatry 64, 577–582.

Amr, M., Raddad, D., El-Mehesh, F., Mahmoud, E.-H., El-Gilany, A-H., 2011. Sex differences in Arab children with Autism spectrum disorders. Res. Autism Spectr. Disord. 5, 1343–1350.

Amr, M., Raddad, D., El-Mehesh, F., Bakr, A., Sallam, K., Amin, T., 2012. Comorbid psychiatric disorders in Arab children with autism spectrum disorders. Res. Autism Spectr. Disord. 6, 240–248.

Ankenman, K., Elgin, J., Sullivan, K., Vincent, L., Bernier, R., 2014. Nonverbal and verbal cognitive discrepancy profiles in autism spectrum disorders: Influence of age and gender. Am. J. Intellect. Dev. Disabil. 119, 84–99.

Anney, R.J.L, Ripke, S., Anttila, V., Grove, J., Holmans, P., Huang, H., et al., 2017. Meta-analysis of GWAS of over 16,000 individuals with autism spectrum disorder highlights a novel locus at 10q24.32 and a significant overlap with schizophrenia. Mol. Autism. 8, 1.

Auyeung, B., Wheelwright, S., Allison, C., Atkinson, M., Samarawickrema, N., Baron-Cohen, S., 2009a. The children's empathy quotient and systemizing quotient: Sex differences in typical development and in autism spectrum conditions. J. Autism Dev. Disord. 39, 1509–1521.

Auyeung, B., Baron-Cohen, S., Ashwin, E., Knickmeyer, R., Taylor, K., Hackett, G., 2009. Fetal testosterone and autistic traits. Br. J. Psychol. 100, 1–22.

Ayhan, F., Konopka, G., 2018. Regulatory genes and pathways disrupted in autism spectrum disorders. Prog. Neuropsychopharmacol. Biol. Psychiatry, 89, 57–64.

Backer van Ommeren, T.B., Koot, H.M., Scheeren, A.M., Begeer, S., 2017. Sex differences in the reciprocal behaviour of children with autism. Autism 21, 795–803.

Baghdadli, A., Pascal, C., Grisi, S., Aussilloux, C., 2003. Risk factors for self-injurious behaviours among 222 young children with autistic disorders. J. Intellect. Disabil. Res. 47, 622–627.

Baio J., Wiggins L., Christensen D. L., 2018. Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014. MMWR Surveill. Summ. 67, 1–23.

Banach, R., Thompson, A., Szatmari, P., Goldberg, J., Tuff, L., Zwaigenbaum, L., Mahoney, W., 2009. Brief report: Relationship between non-verbal IQ and gender in autism. J. Autism Dev. Disord. 39, 188–193.

Baron-Cohen, S., Bowen, D.C., Holt, R. J., Allison, C., Auyeung, B., Lombardo, M.V., Smith, P., Lai, M., 2015. The "reading the mind in the eyes" test: Complete absence of typical sex difference in 400 men and women with autism. PLoS ONE, 10.

Baron-Cohen, S., Cassidy, S., Auyeung, B., Allison, C., Achoukhi, M., Robertson, S., Pohl, A., Lai, M.-C., 2014. Attenuation of typical sex differences in 800 adults with autism vs. 3,900 controls. PLoS ONE, 9.

Baron-Cohen, S., Lombardo, M.V., Auyeung, B., Ashwin, E., Chakabarti, B. & Knickmeyer, R., 2011. Why Are Autism Spectrum Conditions More Prevalent in Males? PLoS Biology, 9, e1001081

Baron-Cohen, S., Wheelwright, S., 2003a. The Friendship Questionnaire: An Investigation of Adults with Asperger Syndrome or High-Functioning Autism, and Normal Sex Differences. J. Autism Dev. Disord. 33, 509–517.

Baron-Cohen, S., Richler, J., Bisarya, D., Gurunathan, N., Wheelwright, S., 2003b. The systemizing quotient: An investigation of adults with Asperger syndrome or high-functioning autism, and normal sex differences. Philos. Trans. R. Soc. B Biol. Sci. 358, 361–374.

Baron-Cohen, S., 2002. The extreme male brain theory of autism. Trends Cogn. Sci. 6, 248-254.

Beacher, F.D., Minati, L., Baron-Cohen, S., Lombardo, M.V., Lai, M.-C., Gray, M.A., Harrison, N. A., Critchley, H. D., 2012a. Autism attenuates sex differences in brain structure: A combined voxel-based morphometry and diffusion tensor imaging study. Am. J. Neuroradiol. 33, 83–89.

Beacher, F.D. Radulescu, E., Minati, L., Baron-Cohen, S., Lombardo, M.V., Lai, M.-C., Walker, A., Howard, D., Gray, M.A., Harrison, N.A., Critchley, H.D., 2012b. Sex differences and Autism: Brain function during verbal fluency and mental rotation. PLoS ONE, 7.

Ben-Itzchak, E., Ben-Shachar, S., Zachor, D.A., 2013. Specific neurological phenotypes in autism spectrum disorders are associated with sex representation. Autism. Res. 6, 596–604.

Bejerot, S., Eriksson, J.M., Bonde, S., Carlstrom, K., Humble, M.B., Eriksson, E., 2012. The extreme male brain revisited: Gender coherence in adults with autism spectrum disorder. Br. J. Psychiatry 201, 116–123.

Blackmon, K., Bluvstein, J., MacAllister, W.S., Avallone, J., Misajon, J., Hedlund, J., Goldberg, R., Bojko, A., Mitra, N., Giridharan, R., Sultan, R., Keller, S., Devinsky, O., 2016. Treatment Resistant Epilepsy in Autism Spectrum Disorder: Increased Risk for Females. Autism. Res., 9, 311–320.

Bloss, C.S., Courchesne, E., 2007. MRI neuroanatomy in young girls with autism: a preliminary study. J. Am. Acad. Child Adolesc. Psychiatry 46, 515–523.

Bolton, P.F., Carcani-Rathwell, I., Hutton, J., Goode, S., Howlin, P., Rutter, M., 2011. Epilepsy in autism: Features and correlates. Br. J. Psychiatry 198, 289–294.

Bölte, S., Duketis, E., Poustka, F., Holtmann, M., 2011. Sex differences in cognitive domains and their clinical correlates in higher-functioning autism spectrum disorders. Autism 15, 497-511.

Calderoni, S., Retico, A., Biagi, L., Tancredi, R., Muratori, F., Tosetti, M., 2012. Female children with autism spectrum disorder: an insight from mass-univariate and pattern classification analyses. Neuroimage 59, 1013–1022.

Campbell, D.J., Chang, J., Chawarska, K., 2014. Early generalized overgrowth in autism spectrum disorder: Prevalence rates, gender effects, and clinical outcomes. J. Am. Acad. Child Adolesc. Psychiatry 53, 1063–1073.

Cantor, R.M., Kono, N., Duvall, J.A., Alvarez-Retuerto, A., Stone, J.L., Alarcón, M., Nelson, S.F., Geschwind, D.H., 2005. Replication of autism linkage: Fine-mapping peak at 17q21. Am. J. Hum. Genet. 76, 1050–1056.

Carayol, J., Schellenberg, G.D., Dombroski, B., Genin, E., Rousseau, F., Dawson, G., 2011. Autism risk assessment in siblings of affected children using sex-specific genetic scores. Mol. Autism, 2.

Carter, A.S., Black, D.O., Tewani, S., Connolly, C.E., Kadlec, M.B., Tager-Flusberg, H., 2007a. Sex differences in toddlers with autism spectrum disorders. J. Autism Dev. Disord. 37, 86–97.

Carter, C.S., 2007b. Sex differences in oxytocin and vasopressin: Implications for autism spectrum disorders? Behav. Brain Res. 176, 170–186.

Cederlöf, M., Gotby, A.O., Larsson, H., Serlachius, E., Boman, M., Långström, N., Landén, M., Lichtenstein, P. 2014. Klinefelter syndrome and risk of psychosis, autism and ADHD. J. Psychiatr. Res. 48, 128–130.

Cermak, S.A., Curtin, C., Bandini, L.G., 2010. Food Selectivity and Sensory Sensitivity in Children with Autism Spectrum Disorders. J. Am. Diet. Assoc. 110, 238–246.

Chakrabarti, B., Dudbridge, F., Kent, L., Wheelwright, S., Hill-Cawthorne, G., Allison, C., Banerjee-Basu, S., Baron-Cohen, S., 2009. Genes related to sex steroids, neural growth, and social-emotional behavior are associated with autistic traits, empathy, and Asperger syndrome. Autism Res. 2, 157–177.

Chakraborti, B., Verma, D., Karmakar, A., Jaiswal, P., Sanyal, A., Paul, D., Sinha, S., Singh, A.S., Guhathakurta, S., Roychowdhury, A., Panda, C.K., Ghosh, S., Mohanakumar, K.P., Mukhophadhyay, K., Rajamma, U., 2016. Genetic variants of MAOB affect serotonin level and specific behavioral attributes to increase autism spectrum disorder (ASD) susceptibility in males. Prog. Neuropsychopharmacol. Biol. Psychiatry 71, 123–136.

Chang, S.-C., Pauls, D.L., Lange, C., Sasanfar, R., Santangelo, S.L., 2013. Sex-specific association of a common variant of the XG gene with autism spectrum disorders. Am. J. Med. Genet. Part B Neuropsychiatr. Genet. 162, 742–750.

Chen, C., Van Horn, J.D., GENDAAR Research Consortium, 2017. Developmental neurogenetics and multimodal neuroimaging of sex differences in autism. Brain Imaging Behav. 11, 38–61.

Cherskov, A., Pohl, A., Allison, C., Zhang, H., Payne, R.A., Baron-Cohen, S. 2018. Polycystic ovary syndrome and autism: A test of the prenatal sex steroid theory. Transl. Psychiatry, 8, 136.

Christenssen, D. L., Baio, J., Van Naarden Braun, K., Bilder, D., Charles, J., Constantion, J. N., Daniels, J., Durkin, M S., Fitzgerald, R., Kurzius-Spencer, M., Lee, L-C., Pettygrove, S., Robinson, C., Schulz, E., Wells, C., Wingate, M. S., Zahorodny, W. & Yeargin-Allsopp, M., 2016. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2012. Surveill. Summ. 65.

Coffman, M.C., Anderson, L.C., Naples, A.J., McPartland, J.C., 2015. Sex differences in social perception in children with ASD. J. Autism Dev. Disord. 45, 589–599.

Cohen, I.L., Tsiouris, J.A., Flory, M.J., Kim, S., Freedland, R., Heaney, G., Pettinger, J., Ted Brown, W., 2010. A large scale study of the psychometric characteristics of the IBR Modified Overt Aggression Scale: Findings and evidence for increased self-destructive behaviors in adult females with autism spectrum disorder. J. Autism Dev. Disord. 40, 599–609.

Craig, M.C., Zaman, S.H., Daly, E.M., Cutter, W.J., Robertson, D.M.W., Hallahan, B., Toal, F., Reed, S., Ambikapathy, A., Brammer, M., Murphy, C.M., Murphy, D.G.M., 2007. Women with autistic-spectrum disorder: Magnetic resonance imaging study of brain anatomy. Br. J. Psychiatry 191, 224-228.

Craig, F., Margari, F., Legrottaglie, A.R., Palumbi, R., de Giambattista, C. & Margari, L., 2016. A review of executive function deficits in autism spectrum disorder and attention-deficit/hyperactivity disorder. Neuropsych. Dis. Treat. 12, 1191–1202.

Daniel, A.M. & Mandell, D.S., 2014. Explaining differences in age at autism spectrum disorder diagnosis: A critical review. Autism. 18. 583–597.

Dean, M., Kasari, C., Shih, W., Frankel, F., Whitney, R., Landa, R., Lord, C., Orlich, F., King, B., Harwood, R., 2014. The peer relationships of girls with ASD at school: Comparison to boys and girls with and without ASD. J. Child Psychol. Psychiatry 55, 1218–1225.

Dean, M., Harwood, R., Kasari, C., 2017. The art of camouflage: Gender differences in the social behaviors of girls and boys with autism spectrum disorder. Autism 21, 678–689.

De Jong, M., Punt, M., De Groot, E., Minderaa, R.B., Hadders-Algra, M., 2011. Minor neurological dysfunction in children with autism spectrum disorder. Dev. Med. Child Neurol. 53, 641–646.

Domes, G., Heinrichs, M., Kumbier, E., Grossmann, A., Hauenstein, K., Herpertz, S.C., 2013. Effects of intranasal oxytocin on the neural basis of face processing in autism spectrum disorder. Biol. Psychiatry 74, 164–171.

Duerden, E.G., Oatley, H.K., Mak-Fan, K.M., McGrath, P.A., Taylor, M.J., Szatmari, P., Roberts, S.W., 2012. Risk factors associated with self-injurious behaviors in children and adolescents with autism spectrum disorders. J. Autism Dev. Disord. 42, 2460–2470.

Dumais, K.M., Veenema, A.H., 2016. Vasopressin and oxytocin receptor systems in the brain: Sex differences and sex-specific regulation of social behavior. Front. Neuroendocrinol. 40, 1–23.

Durdiakova, J., Ostatnikova, D., Celec, P., 2011. Testosterone and its metabolites - modulators of brain functions. Acta Neurobiol. Exp. 71, 434–454.

Duvekot, J., van der Ende, J., Verhulst, F.C., Slappendel, G., van Daalen, E., Maras, A., GreavesLord, K., 2017. Factors influencing the probability of a diagnosis of autism spectrum disorder in girls versus boys. Autism 21, 646–658.

Ecker, C., Bookheimer, S. Y. & Murphy, D.G., 2015. Neuroimaging in autism spectrum disorder: brain structure and function across the lifespan. Lancet Neurol. 14, 1121–1134.

Ecker, C., Andrews, D.S., Gudbrandsen, C.M., Marquand, A.F., Ginestet, C.E., Daly, E.M., Murphy, C.M., Lai, M., Lombardo, M.V., Ruigrok, A.N.V., Bullmore, E.T., Suckling, J., Williams, S.C.R., Baron-Cohen, S., Craig, M.C., Murphy, D.G.M., 2017. Association Between the Probability of Autism Spectrum Disorder and Normative Sex-Related Phenotypic Diversity in Brain Structure. JAMA Psychiatry 74, 329–338.

Edens, A.C., Lyons, M.J., Duron, R.M., Dupont, B.R., Holden, K.R., 2011. Autism in two females with duplications involving Xp11.22-p11.23. Dev. Med. Child Neurol. 53, 463–466.

Frazier, T.W., Georgiades, S., Bishop, S.L., Hardan, A.Y., 2014. Behavioral and cognitive characteristics of females and males with autism in the Simons Simplex Collection. J. Am. Acad. Child Adolesc. Psychiatry 53, 329–340.

Fox P.T., Lancaster J.L., 2002. Mapping context and content: The BrainMap model. Nature Rev. Neurosci. 3, 319–321.

Fulton, A.M., Paynter, J.M., Trembath, D., 2017. Gender comparisons in children with ASD entering early intervention. Res. Dev. Disabil. 68, 27–34.

Gadow, K.D., DeVincent, C.J., 2012. Comparison of children with autism spectrum disorder with and without schizophrenia spectrum traits: Gender, season of birth, and mental health risk factors. J. Autism Dev. Disord. 42, 2285–2296.

Geier, D.A., Geier, M.R., 2007. A prospective assessment of androgen levels in patients with autistic spectrum disorders: biochemical underpinnings and suggested therapies. Neuroendocrinol. Lett. 28, 565–573.

Giarelli, E., Wiggins, L., Rice, C.E., Levy, S. E., Kirby, R.S., Pinto-Martin, J. & Mandell, D., 2010. Sex differences in the evaluation and diagnosis of autism spectrum disorders among children. Disabil. Health. 3, 107–116.

Gilani, S.Z., Tan, D.W., Russell-Smith, S.N., Maybery, M.T., Mian, A., Eastwood, P.R., Shafait, F., Goonewardene, M., Whitehouse, A.J.O., 2015. Sexually dimorphic facial features vary according to level of autistic-like traits in the general population. J. Neurodev. Disord. 7.

Gockley, J., Willsey, A.J., Dong, S., Dougherty, J.D., Constantino, J.N., Sanders, S.J., 2015. The female protective effect in autism spectrum disorder is not mediated by a single genetic locus Dr Meng-Chuan Lai. Mol. Autism 6.

Goddard, L., Dritschel, B., Howlin, P., 2014. A preliminary study of gender differences in autobiographical memory in children with an autism spectrum disorder. J. Autism Dev. Disord. 44, 2087–2095.

Gong, X., Bacchelli, E., Blasi, F., Toma, C., Betancur, C., Chaste, P., Delorme, R., Durand, C.M., Fauchereau, F., Botros, H.G., Leboyer, M., Mouren-Simeoni, M.-C., Nygren, G., Anckarsäter, H., Rastam, M., Gillberg, I.C., Gillberg, C., Moreno-De-Luca, D., Carone, S., Nummela, I., Rossi, M., Battaglia, A., Jarvela, I., Maestrini, E., Bourgeron, T., 2008. Analysis of X chromosome inactivation in autism spectrum disorders. Am. J. Med. Genet. Part B Neuropsychiatr. Genet. 147, 830–835.

Grove, R., Hoekstra, R.A., Wierda, M., Begeer, S., 2017. Exploring sex differences in autistic traits: A factor analytic study of adults with autism. Autism 21, 760–768.

Guastella, A.J., Einfeld, S.L., Gray, K.M., Rinehart, N.J., Tonge, B.J., Lambert, T.J., Hickie, I.B., 2010. Intranasal Oxytocin Improves Emotion Recognition for Youth with Autism Spectrum Disorders. Biol. Psychiatry 67, 692–694.

Haney, J.L., 2016. Autism, females, and the DSM-5: Gender bias in autism diagnosis. Soc. Work Ment. Healt, 14, 396-407.

Happé, F. & Frith, U., 2006. The Weak Coherence Account: Detail-focused Cognitive Style in Autism Spectrum Disorders. J. Autism Dev. Disord., 36, 5–25.

Harrop, C., Shire, S., Gulsrud, A., Chang, Y., Ishijima, E., Lawton, K., Kasari, C., 2015a. Does gender influence core deficits in ASD? An investigation into social-communication and play of girls and boys with ASD. J. Autism Dev. Disord. 45, 766–777.

Harrop, C., Gulsrud, A., Kasari, C., 2015b. Does gender moderate core deficits in ASD? An investigation into restricted and repetitive behaviors in girls and boys with ASD. J. Autism Dev. Disord. 45, 3644–3655.

Hartley, S.L., Sikora, D.M., 2009. Sex differences in Autism spectrum disorder: An examination of developmental functioning, Autistic symptoms, and coexisting behavior problems in toddlers. J. Autism Dev. Disord,. 39, 1715–1722.

Hattier, M.A., Matson, J.L., Tureck, K., Horovitz, M., 2011. The effects of gender and age on repetitive and/or restricted behaviors and interests in adults with autism spectrum disorders and intellectual disability. Res. Dev. Disabil. 32, 2346–2351.

Head, A.M., McGillivray, J.A., Stokes, M.A., 2014. Gender differences in emotionality and sociability in children with autism spectrum disorders. Mol. Autism 5.

Henningsson, S., Jonsson, L., Ljunggren, E., Westberg, L., Gillberg, C., Råstam, M., Anckarsäter, H., Nygren, G., Landn, M., Thuresson, K., Betancur, C., Leboyer, M., Gillberg, C., Eriksson, E., Melke, J., 2009. Possible association between the androgen receptor gene and autism spectrum disorder. Psychoneuroendocrinology 34, 752–761.

Hill, E.L., 2004. Executive dysfunction in autism. Trends Cogn. Sci. 8, 26–32.

Hiller B., Bradtke J., Balz H., Rieder H., 2004. "CyDAS Online Analysis Site", http://www.cydas.org/OnlineAnalysis/

Hiller, R.M., Young, R.L., Weber, N., 2014. Sex Differences in Autism Spectrum Disorder based on DSM-5 Criteria: Evidence from Clinician and Teacher Reporting. J. Abnorm. Child Psychol. 42, 1381–1393.

Hobson, R. P., 1986. The autistic child's appraisal of expressions of emotion. J. Child Psychol. Psychiatry, 27, 321–342.

Holtmann, M., Bölte, S., Poustka, F., 2007. Autism spectrum disorders: Sex differences in autistic behaviour domains and coexisting psychopathology. Dev. Med. Child Neurol. 49, 361–366.

Hu, V.W., Sarachana, T., Sherrard, R.M., Kocher, K.M., 2015. Investigation of sex differences in the expression of RORA and its transcriptional targets in the brain as a potential contributor to the sex bias in autism. Mol. Autism 6.

Idring, S., Lundberg, M., Strum, H., Dalman, C., Gumpert, C., Rai, D., Lee, B.K., Magnusson, C., 2015. Changes in Prevalence of Autism Spectrum Disorders in 2001–2011: Findings from the Stockholm Youth Cohort. J. Autism Dev. Disord. 45, 1766–1773.

Ingudomnukul, E., Baron-Cohen, S., Wheelwright, S., Knickmeyer, R., 2007. Elevated rates of testosterone-related disorders in women with autism spectrum conditions. Horm. Behav. 51, 597–604.

Iossifov I., O'Roak B.J., Sanders S.J., Ronemus M., Krumm N., Levy D., Stessman H.A., Witherspoon K.T., Vives L., Patterson K.E., Smith J.D., Paeper B., Nickerson D.A., Dea J., Dong S., Gonzalez L.E., Mandell J.D., Mane S.M., Murtha M.T., Sullivan C.A., Walker M.F., Waqar Z., Wei L., Willsey A.J., Yamrom B., Lee Y.H., Grabowska E., Dalkic E., Wang Z., Marks S., Andrews P., Leotta A., Kendall J., Hakker I., Rosenbaum J., Ma B., Rodgers L., Troge J., Narzisi G., Yoon S1, Schatz M.C., Ye K., McCombie W.R., Shendure J., Eichler E.E., State M.W., Wigler M., 2014. The contribution of de novo coding mutations to autism spectrum disorder. Nature, 515, 216–221.

Jacquemont, S., Coe, B.P., Hersch, M., Duyzend, M.H., Krumm, N., Bergmann, S., Beckmann, J.S., Rosenfeld, J.A., Eichler, E.E., 2014. A higher mutational burden in females supports a "female protective model" in neurodevelopmental disorders. Am. J. Hum. Genet. 94, 415–425.

Joseph, L., Thurm, A., Farmer, C., Shumway, S., 2013. Repetitive behavior and restricted interests in young children with autism: Comparisons with controls and stability over 2 years. Autism Res. 6, 584–595.

Kaartinen, M., Puura, K., Helminen, M., Salmelin, R., Pelkonen, E., Juujärvi, P., 2014. Reactive aggression among children with and without autism spectrum disorder. J. Autism Dev. Disord. 44, 2383–2391.

Kanner, L., 1943. Autistic Disturbances of Affective Contact. Nervous Child 2, 217–50.

Kiep, M., Spek, A.A., 2017. Executive functioning in men and women with an autism spectrum disorder. Autism Res. 10, 940–948.

Kirkovski, M., Enticott, P.G., Fitzgerald, P.B., 2013. A review of the role of female gender in autism spectrum disorders. J. Autism Dev. Disord. 43, 2584–2603.

Kirkovski, M., Enticott, P.G., Maller, J.J., Rossell, S.L., Fitzgerald, P.B., 2015. Diffusion tensor imaging reveals no white matter impairments among adults with autism spectrum disorder. Psychiatry Res. 233, 64-72.

Kirkovski, M., Enticott, P.G., Hughes, M.E., Rossell, S.L., Fitzgerald, P.B., 2016. Atypical neural activity in males but not females with autism spectrum disorder. J. Autism Dev. Disord. 46, 954–963.

Knickmeyer, R., Baron-Cohen, S., Fane, B.A., Wheelwright, S., Mathews, G.A., Conway, G.S., Brook, C.G.D., Hines, M., 2006. Androgens and autistic traits: A study of individuals with congenital adrenal hyperplasia. Horm. Behav. 50, 148–153.

Konstantareas, M.M., Homatidis, S., Busch, J., 1989. Cognitive, communication, and social differences between autistic boys and girls. J. Appl. Dev. Psychol. 10, 411–424.

Kozlowski, A.M., Matson, J.L., Rieske, R.D., 2012. Gender effects on challenging behaviors in children with autism spectrum disorders. Res. Autism Spectr. Disord. 6, 958–964.

Krahn, T.M., Fenton, A., 2012. The extreme male brain theory of autism and the potential adverse effects for boys and girls with autism. J. Bioeth. Inq., 9, 93–103.

Kumazaki, H., Muramatsu, T., Kosaka, H., Fujisawa, T.X., Iwata, K., Tokoda, A., Tsuchiya, K., Mimura, M., 2015. Sex differences in cognitive and symptom profiles in children with high functioning autism spectrum disorders. Res. Autism Spectr. Disord. 13-14, 1–7.

Lai, M.-C., Lombardo, M.V., Pasco, G., Ruigrok, A.N.V., Wheelwright, S.J., Sadek, S.A., Chakrabarti, B., Baron-Cohen, S., MRC AIMS Consortium, 2011. A behavioral comparison of male and female adults with high functioning autism spectrum conditions. PLoS ONE 6, 10.

Lai, M.-C., Lombardo, M.V., Ruigrok, A.N.V., Chakrabarti, B., Wheelwright, S.J., Auyeung, B., Allison, C., Baron-Cohen, S., MRC AIMS Consortium, 2012. Cognition in males and females with autism: Similarities and differences. PLoS ONE 7, 15.

Lai, M.-C., Lombardo, M.V., Suckling, J., Ruigrok, A.N.V., Chakrabarti, B., Ecker, C., Deoni, S.C.L., Craig, M.C., Murphy, D.G.M., Bullmore, E.T., Baron-Cohen, S., 2013. Biological sex affects the neurobiology of autism. Brain 136, 2799–2815.

Lai, M.-C., Lerch, J.P., Floris, D. L., Ruigrok, A.N.V., Pohl, A., Lombardo, M.V., Baron-Cohen, S., 2017a. Imaging Sex/Gender and Autism in the Brain: Etiological Implications. J. Neurosci. Res. 95, 380–397

Lai, M.-C., Lombardo, M.V., Ruigrok, A.N.V., Chakrabarti, B., Auyeung, B., Szatmari, P., Happe, F., Baron-Cohen, S., 2017b. Quantifying and exploring camouflaging in men and women with autism. Autism 21, 690–702.

Lainhart, J.E., Piven, J., Wzorek, M., Landa, R., Santangelo, S.L., Coon, H., Folstein, S.E., 1997. Macrocephaly in children and adults with autism. J. Am. Acad. Child Adolesc. Psychiatry 36, 282–290.

Lamb, J.A., Barnby, G., Bonora, E., Sykes, N., Bacchelli, E., Blasi, F., Maestrini, E., Broxholme, J., Tzenova, J., Weeks, D., Bailey, A.J., Monaco, A.P., 2005. Analysis of IMGSAC autism susceptibility loci: evidence for sex limited and parent of origin specific effects. J. Med. Genet. 42, 132–137.

Lehnhardt, F., Falter, C.M., Gawronski, A., Pfeiffer, K., Tepest, R., Franklin, J., Vogeley, K., 2016. Sex-related cognitive profile in autism spectrum disorders diagnosed late in life: Implications for the female autistic phenotype. J. Autism Dev. Disord. 46, 139–154.

Lemon, J.M., Gargaro, B., Enticott, P.G., Rinehart, N.J., 2011. Brief report: Executive functioning in autism spectrum disorders: A gender comparison of response inhibition. J. Autism Dev. Disord. 41, 352–356.

Levy, D., Ronemus, M., Yamrom, B., Lee, Y., Leotta, A., Kendall, J., Marks, S., Lakshmi, B., Pai, D., Ye, K., Buja, A., Krieger, A., Yoon, S., Troge, J., Rodgers, L., Iossifov, I., Wigler, M., 2011. Rare De Novo and Transmitted Copy-Number Variation in Autistic Spectrum Disorders. Neuron 70, 886–897.

Liberati, A., Altman, D. G., Tetzlaff, J., Mulrow, C., Gotzsche, P. C., & Ioannidis, J. P. A., 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: Explanation and elaboration. BMJ, 339, b2700.

Livingston, L.A., Emma, C., Patrick, B., Happé F., 2018. Good social skills despite poor theory of mind: exploring compensation in autism spectrum disorder. J Child Psychol. Psychiatr.

Lord, C., Schopler, E., Revicki, D., 1982. Sex differences in autism. J. Autism Dev. Disord. 12, 317–330.

Magiati, I., Ong, C., Lim, X.Y., Tan, J.W., Ong, A.Y.L., Patrycia, F., Fung, D.S.S., Sung, M., Poon, K.K., Howlin, P., 2016. Anxiety symptoms in young people with autism spectrum disorder attending special schools: Associations with gender, adaptive functioning and autism symptomatology. Autism 20, 306–320.

Mandic-Maravic, V., Pejovic-Milovancevic, M., Mitkovic-Voncina, M., Kostic, M., Aleksic-Hil, O., Radosavljev-Kircanski, J., Mincic, T., Lecic-Tosevski, D., 2015. Sex differences in Autism spectrum disorders: Does sex moderate the pathway from clinical symptoms to adaptive behavior? Sci. Rep. 5.

Mandy, W., Chilvers, R., Chowdhury, U., Salter, G., Seigal, A., Skuse, D., 2012. Sex differences in autism spectrum disorder: Evidence from a large sample of children and adolescents. J. Autism Dev. Disord. 42, 1304–1313.

Marco, E. J., Skuse, D. H. 2006. Autism-lessons from the X chromosome. SCAN, 1, 183–193.

May, T., Cornish, K., Rinehart, N., 2014. Does gender matter? A one year follow-up of autistic, attention and anxiety symptoms in high-functioning children with autism spectrum disorder. J. Autism Dev. Disord. 44, 1077–1086.

May, T., Cornish, K., Rinehart, N.J., 2016. Gender Profiles of Behavioral Attention in Children with Autism Spectrum Disorder. J. Atten. Disord. 20, 627–635.

Mayes, S.D., Calhoun, S.L., Aggarwal, R., Baker, C., Mathapati, S., Molitoris, S., Mayes, R.D., 2013. Unusual fears in children with autism. Res. Autism Spectr. Disord. 7, 151-158.

McLennan, J.D., Lord, C., Schopler, E., 1993. Sex differences in higher functioning people with autism. J. Autism Dev. Disord. 23, 217–227.

Memari, A.H., Ziaee, V., Shayestehfar, M., Ghanouni, P., Mansournia, M.A., Moshayedi, P., 2013. Cognitive flexibility impairments in children with autism spectrum disorders: Links to age, gender and child outcomes. Res. Dev. Disabil. 34, 3218–3225.

Miller, M., Bales, K.L., Taylor, S.L., Yoon, J., Hostetler, C.M., Carter, C.S., Solomon, M., 2013. Oxytocin and Vasopressin in Children and Adolescents with Autism Spectrum Disorders: Sex Differences and Associations with Symptoms. Autism Res. 6, 91–102.

Mitra, I., Tsang, K., Ladd-Acosta, C., Croen, L.A., Aldinger, K.A., Hendren, R.L., Traglia, M., Lavillaureix, A., Zaitlen, N., Oldham, M.C., Levitt, P., Nelson, S., Amaral, D.G., Herz-Picciotto, I., Fallin, M.D., Weiss, L.A., 2016. Pleiotropic Mechanisms Indicated for Sex Differences in Autism. PLoS Genet. 12.

Mody, M. & Belliveau, J. W., 2013. Speech and language impairments in Autism: Insights from behavior and neuroimaging. N. Am. J. Med. Sci. 5, 157–161.

Mussey, J.L., Ginn, N.C., Klinger, L.G., 2017. Are males and females with autism spectrum disorder more similar than we thought? Autism 21, 733–737.

Nava, C., Lamari, F., Héron, D., Mignot, C., Rastetter, A., Keren, B., Cohen, D., Faudet, A., Bouteiller, D., Gilleron, M., Jacquette, A., Whalen, S., Afenjar, A., Périsse, D., Laurent, C., Dupuits, C., Gautier, C., Gérad, M., Caillet, S., Leheup, B., Leboyer, M., Gillber, C., Delorme, R., Bourgeron, T., Brice, A., Depienne, C., 2012. Analysis of the chromosome X exome in patients with autism spectrum disorders identified novel candidate genes, including TMLHE. Transl Psychiatry, 2, e179.

Nordahl, C.W., Iosif, A.-M., Young, G.S., Perry, L.M., Dougherty, R., Lee, A., Li, D., Buonocore, M.H., Simon, T., Rogers, S., Wandell, B., Amaral, D.G., 2015. Sex differences in the corpus callosum in preschool-aged children with autism spectrum disorder. Mol. Autism 6.

O´Connor, K., 2012. Auditory processing in autism spectrum disorder: A review. Neurosci. Biobehav. Rev. 36, 836-854.

Oliveira G., Ataide A., Marques C., Miguel, T. S., Mota-Vieira, L., Gonçalves, E., Lopes, N. M., Rodrigues, V., da Mota, H. C. & Vicente, A. M., 2007. Epidemiology of autism spectrum disorder in Portugal: prevalence, clinical characterization, and medical conditions. Dev Med Child Neurol. 49,726–733.

Ormond, S., Brownlow, C., Garnett, M.S., Rynkiewicz, A., Attwood, T., 2018. Profiling Autism Symptomatology: An Exploration of the Q-ASC Parental Report Scale in Capturing Sex Differences in Autism. J. Autism Dev. Disord. 48, 389–403.

Oswald, T.M., Winter-Messiers, M.A., Gibson, B., Schmidt, A.M., Herr, C.M., Solomon, M., 2016. Sex Differences in Internalizing Problems During Adolescence in Autism Spectrum Disorder. J. Autism Dev. Disord. 46, 624-636.

Oteify, G., El-Ramly, A., Samy, A. & Soliman, E., 2018. Evaluation of oxytocin and serotonin levels in autism spectrum disorder. J. Med. Sci. Res. 1, 66–71.

Palmer, N., Beam, A., Agniel, D., Eran, A., Manrai, A., Spettell, C., Steinberg, G., Mandl, K., Fox, K., Nelson, S.F., Kohane, I., 2017. Association of sex withrecurrence of Autism Spectrum Disorder among siblings. JAMA Pediatrics 171, 1107-1112.

Park, S., Cho, S.-C., Cho, I.H., Kim, B.-N., Kim, J.-W., Shin, M.-S., Chung, U.-S., Park, T.-W., Son, J.-W., Yoo, H.J., 2012. Sex differences in children with autism spectrum disorders compared with their unaffected siblings and typically developing children. Res. Autism Spectr. Disord. 6, 861–870.

Paul, R., Klin, A., Volkmar, F. R. 2005. Perception and production of prosody by speakers with Autism Spectrum Disorders. J. Autism Dev. Disord. 35, 205–220.

Persico, A. M. & Napolioni, V., 2013. Autism genetics. Behav. Brain Res. 251, 95–112.

Philip, R. C. M., Dauvermann, M. R., Whalley, H. C., Baynham, K., Lawrie, S. M., Stanfield, A. C., 2012. A systematic review and meta-analysis of the fMRI investigation of autism spectrum disorders. Neurosci. Biobehav. Rev. 36, 901–942.

Pisula, E., Kawa, R., Szostakiewicz, L., Lucka, I., Kawa, M., Rynkiewicz, A., 2013. Autistic traits in male and female students and individuals with high functioning autism spectrum disorders measured by the Polish version of the Autism-Spectrum Quotient. PLoS ONE, 8, e75236.

Pisula, E., Pudlo, M., Slowinska, M., Kawa, R., Strzaska, M., Banasiak, A., Wolanczyk, T., 2017. Behavioral and emotional problems in high-functioning girls and boys with autism spectrum disorders: Parents' reports and adolescents' self-reports. Autism 21, 738–748.

Piven, J., Arndt, S., Bailey, J., Andreasen, N., 1996. Regional brain enlargement in autism: a magnetic resonance imaging study. J. Am. Acad. Child Adolesc. Psychiatry. 35, 530–536.

Pohl, A., Cassidy, S., Auyeung, B., Baron-Cohen, S., 2014. Uncovering steroidopathy in women with autism: A latent class analysis. Mol. Autism 5.

Postorino, V., Fatta, L.M., De Peppo, L., Giovagnoli, G., Armando, M., Vicari, S., Mazzone, L., 2015. Longitudinal comparison between male and female preschool children with autism spectrum disorder. J. Autism Dev. Disord. 45, 2046-2055.

Postorino, V., Scahill, L., De Peppo, L., Fatta, L.M., Zanna, V., Castiglioni, M.C., Gillespie, S., Vicari, S., Mazzone, L., 2017. Investigation of Autism Spectrum Disorder and Autistic Traits in an Adolescent Sample with Anorexia Nervosa. J. Autism Dev, Disor. 47, 1051–1061.

Øien, R.A., Vambheim, S.M., Hart, L., Nordahl-Hansen, A., Erickson, C., Wink, L., Eisemann, M.R., Shic, F., Volkmar, F.R., Grodberg, D., 2018. Sex-Differences in Children Referred for Assessment: An Exploratory Analysis of the Autism Mental Status Exam (AMSE). J. Autism Dev. Disord. 1–7.

Reinhardt, V.P., Wetherby, A.M., Schatschneider, C., Lord, C., 2015. Examination of Sex Differences in a Large Sample of Young Children with Autism Spectrum Disorder and Typical Development. J. Autism Dev. Disord. 45, 697–706.

Retico, A., Giuliano, A., Tancredi, R., Cosenza, A., Apicella, F., Narzisi, A., Biagi, L., Tosetti, M., Muratori, F., Calderoni, S., 2016. The effect of gender on the neuroanatomy of children with autism spectrum disorders: a support vector machine case-control study. Mol. Autism. 7, 5.

Review Manager (RevMan) (Computer program). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Rivet, T.T., Matson, J.L., 2011a. Review of gender differences in core symptomatology in autism spectrum disorders. Res. Autism Spectr. Disord. 5, 957–976.

Rivet, T.T., Matson, J.L., 2011b. Gender Differences in Core Symptomatology in Autism Spectrum Disorders across the Lifespan. J. Dev. Phys. Disabil. 23, 399–420.

Robinson, E.B., Lichtenstein, P., Anckarsater, H., Happe, F., Ronald, A., 2013. Examining and interpreting the female protective effect against autistic behavior. PNAS 110, 5258–5262.

Ross, L.A., Del Bene, V.A., Molholm, S., Frey, H.-P., Foxe, J.J., 2015. Sex differences in multisensory speech processing in both typically developing children and those on the autism spectrum. Front. Neurosci. 9.

Rubenstein, E., Wiggins, L.D., Lee, L., 2015. A Review of the Differences in Developmental, Psychiatric, and Medical Endophenotypes Between Males and Females with Autism Spectrum Disorder. J. Dev. Physic. Disabil. 27, 119–139.

Rutherford, M., McKenzie, K., Johnson, T., Catchpole, C., O'Hare, A., McClure, I., Forsyth, K., McCartney, D., Murray, A., 2016. Gender ratio in a clinical population sample, age of diagnosis and duration of assessment in children and adults with autism spectrum disorder. Autism 20, 628–634.

Rynkiewicz, A., Schuller, B., Marchi, E., Piana, S., Camurri, A., Lassalle, A., Baron-Cohen, S., 2016. An investigation of the 'female camouflage effect' in autism using a computerized ADOS-2 and a test of sex/gender differences. Mol. Autism 7.

Råstam, M., 2008. Eating disturbances in autism spectrum disorders with focus on adolescent and adult years. Clin. Neuropsychiatry 5, 31–42.

Saemundsen E., Magnusson P., Georgsdottir I., Egilsson E., Rafnsson V., 2013. Prevalence of autism spectrum disorders in an Icelandic birth cohort. BMJ Open. 3, e002748.

Sanders, J., Johnson, K.A., Garavan, H., Gill, M., Gallagher, L., 2008. A review of neuropsychological and neuroimaging research in autistic spectrum disorders: Attention, inhibition and cognitive flexibility. Res. Autism Spectr. Disord. 2, 1–16.

Schaafsma, S.M., Pfaff, D.W., 2014. Etiologies underlying sex differences in Autism Spectrum Disorders. Front. Neuroendocrinol. 35, 255–271.

Schaer, M., Kochalka, J., Padmanabhan, A., Supekar, K., Menon, V., 2015. Sex differences in cortical volume and gyrification in autism. Mol. Autism 6.

Schellenberg, G.D., Dawson, G., Sung, Y.J., Estes, A., Munson, J., Rosenthal, E., Rothstein, J., Flodman, P., Smith, M., Coon, H., Leong, L., Yu, C.-E, Stodgell, C., Rodier, P.M., Spence, M.A., Minshew, N., McMahon, W.M., Wijsman, E.M., 2006. Evidence for multiple loci from a genome scan of autism kindreds. Mol. Psychiatry 11, 1049–1060.

Schneider, K., Regenbogen, C., Pauly, K.D., Gossen, A., Schneider, D.A., Mevissen, L., Michel, T.M., Gur, R.C., Habel, U., Schneider, F., 2013. Evidence for gender-specific endophenotypes in high-functioning autism spectrum disorder during empathy. Autism Res. 6, 506–521.

Schuch, J.B., Muller, D., Endres, R.G., Bosa, C.A., Longo, D., Schuler-Faccini, L., Ranzan, J., Becker, M.M., dos Santos Riesgo, R., Roman, T., 2016. Psychomotor agitation and mood instability in patients with autism spectrum disorders: A possible effect of SLC6A4 gene? Res. Autism Spectr. Disord. 26, 48–56.

Schumann, C.M., Barnes, C.C., Lord, C., Courchesne, E., 2009. Amygdala Enlargement in Toddlers with Autism Related to Severity of Social and Communication Impairments. Biol. Psychiatry 66, 942–949.

Schumann, C.M., Bloss, C.S., Barnes, C.C., Wideman, G.M., Carper, R.A., Akshoomoff, N., Pierce, K., Hagler, D., Schork, N., Lord, C., Courchesne, E., 2010. Longitudinal magnetic resonance imaging study of cortical development through early childhood in autism. J. Neurosci. 30, 4419–4427.

Schwarz, E., Guest, P.C., Rahmoune, H., Wang, L., Levin, Y., Ingudomnukul, E., Ruta, L., Kent, L., Spain, M., Baron-Cohen, S., Bahn, S., 2011. Sex-specific serum biomarker patterns in adults with Asperger's syndrome. Mol. Psychiatry 16, 1213–1220.

Sebat, J., Lakshmi, B., Malhotra, D., Troge, J., Lese-Martin, C., Walsh, T., Yamrom, B., Yoon, S., Krasnitz, A., Kendall, J., Leotta, A., Pai, D., Zhang, R., Lee, Y.-H., Hicks, J., Spence, S. J., Lee, A. T., Puura, K., Lehtimäki, T., Ledbetter, D., Gregersen, P. K., Bregman, J., Sutcliffe, J. S., Jobanputra, V., Chung, W., Warburton, D., King, M.-C., Skuse, D., Geschwind, D. H., Gilliam, C., Ye, K. & Wigler, M., 2007. Strong Association of De Novo Copy Number Mutations with Autism. Science 316, 445–449.

Sedgewick, F., Hill, V., Yates, R., Pickering, L., Pellicano, E., 2016. Gender differences in the social motivation and friendship experiences of autistic and non-autistic adolescents. J. Autism Dev. Disord. 46, 1297–1306.

Shattuck, P. T., Durkin, M., Maenner, M., Newschaffer, C., Mandell, D. S., Wiggins, L., Lee, L.-C., Rice, C., Giarelli, E., Kirby, R., Baio, J., Pinto-Martin, J. & Cuniff, C., 2009. The timing of identification among children with an Autism Spectrum Disorder: Findings from a population-based surveillance study. J. Am. Acad. Child. Adolesc. Psychiatry. 48, 474–483.

Simon, L., Kozák, L. R., Simon, V., Unoka, Z., Szabó, Ádám, Csukly, Gábor., 2013. Regional Grey Matter Structure Differences between Transsexuals and Healthy Controls—A Voxel Based Morphometry Study. PLoS One 8, e83947.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., Baird, G., 2008. Psychiatric disorders in children with autism spectrum disorders: Prevalence, comorbidity, and associated factors in a population-derived sample. J. Am. Acad. Child Adolesc. Psychiatry 47, 921–929.

Sipes, M., Matson, J.L., Worley, J.A., Kozlowski, A.M., 2011. Gender differences in symptoms of Autism Spectrum Disorders in toddlers. Res. Autism Spectr. Disord. 5, 1465–1470.

Solomon, M., Miller, M., Taylor, S.L., Hinshaw, S.P., Carter, C.S., 2012. Autism symptoms and internalizing psychopathology in girls and boys with autism spectrum disorders. J. Autism Dev. Disord. 42, 48–59.

Sparks, B.F., Friedman, S.D., Shaw, D.W., Aylward, E.H., Echelard, D., Artru, A.A., Maravilla, K.R., Giedd, J.N., Munson, J., Dawson, G., Dager, S.R., 2002. Brain structural abnormalities in young children with autism spectrum disorder. Neurology 59, 184–192.

Steeb, H., Ramsey, J.M., Guest, P.C., Stocki, P., Cooper, J.D., Rahmoune, H., Ingudomnukul, E., Auyeung, B., Ruta, L., Baron-Cohen, S., Bahn, S., 2014. Serum proteomic analysis identifies sex-specific differences in lipid metabolism and inflammation profiles in adults diagnosed with Asperger syndrome. Mol. Autism 5.

Stone, J.L., Merriman, B., Cantor, R.M., Yonan, A.L., Conrad Gilliam, T., Geschwind, D.H., Nelson, S.F., 2004. Evidence for sex-specific risk alleles in autism spectrum disorder. Am. J. Hum. Genet. 75, 1117–1123.

Strang, J. F., Kenworthy, L., Dominska, A., Sokoloff, J., Kenealy, L. E., Berl, M., Walsh, K., Menvielle, E., Slesaransky-Poe, G., Kim, K.-E., Luong-Tran, C., Meagher, H. & Wallace, G. L., 2014. Increased Gender Variance in Autism Spectrum Disorders and Attention Deficit Hyperactivity Disorder. Arch. Sex Behav. 43, 1525–1533.

Sucksmith, E., Allison, C., Baron-Cohen, S., Chakrabarti, B., Hoekstra, R.A., 2013. Empathy and emotion recognition in people with autism, first-degree relatives, and controls. Neuropsychologia 51, 98–105.

Sun X., Allison C., Auyeung B., Baron-Cohen S., Brayne C., 2014. Parental concerns, socioeconomic status, and the risk of autism spectrum conditions in a population-based study. Res Dev Disabil. 35, 3678–3688.

Supekar, K., Menon, V., 2015. Sex differences in structural organization of motor systems and their dissociable links with repetitive/restricted behaviors in children with autism. Mol. Autism 6.

Szatmari, P., Liu, X.-., Goldberg, J., Zwaigenbaum, L., Paterson, A.D., Woodbury-Smith, M., Georgiades, S., Duku, E., Thompson, A., 2012. Sex differences in repetitive stereotyped behaviors in autism: Implications for genetic liability. Am. J. Med. Genet. Part B Neuropsychiatr. Genet. 159 B, 5–12.

Szatmari, P., Paterson, A.D., Zwaigenbaum, L., Roberts, W., Brian, J., Liu, X.-., Vincent, J.B., Skaug, J.L., Thompson, A.P., Senman, L., Feuk, L., Qian, C., Bryson, S.E., Jones, M.B., Marshall, C.R., Scherer, S.W., Vieland, V.J., Bartlett, C., Mangin, L.V., Goedken, R., Segre, A., Pericak-Vance, M.A., Cuccaro, M.L., Gilbert, J.R., Wright, H.H., Abramson, R.K., Betancur, C., Bourgeron, T., Gillberg, C., Leboyer, M., Buxbaum, J.D., Davis, K.L., Hollander, E., Silverman, J.M., Hallmayer, J., Lotspeich, L., Sutcliffe, J.S., Haines, J.L., Folstein, S.E., Piven, J., Wassink, T.H., Sheffield, V., Geschwind, D.H., Bucan, M., Brown, W.T., Cantor, R.M., Constantino, J.N., Gilliam, T.C., Herbert, M., LaJonchere, C., Ledbetter, D.H., Lese-Martin, C., Miller, J., Nelson, S., Samango-Sprouse, C.A., Spence, S., State, M., Tanzi, R.E., Coon, H., Dawson, G., Devlin, B., Estes, A., Flodman, P., Klei, L., McMahon, W.M., Minshew, N., Munson, J., Korvatska, E., Rodier, P.M., Schellenberg, G.D., Smith, M., Spence, M.A., Stodgell, C., Tepper, P.G., Wijsman, E.M., Yu, C.-E., Rog., B., Mantoulan, C., Wittemeyer, K., Poustka, A., Felder, B., Klauck, S.M., Schuster, C., Poustka, F., Bölte, S., Feineis-Matthews, S., Herbrecht, E., Schmtzer, G., Tsiantis, J., Papanikolaou, K., Maestrini, E., Bacchelli, E., Blasi, F., Carone, S., Toma, C., Van Engeland, H., De Jonge, M., Kemner, C., Koop, F., Langemeijer, M., Hijimans, C., Staal, W.G., Baird, G., Bolton, P.F., Rutter, M.L., Weisblatt, E., Green, J., Aldred, C., Wilkinson, J.-., Pickles, A., Le Couteur, A., Berney, T., McConachie, H., Bailey, A.J., Francis, K., Honeyman, G., Hutchinson, A., Parr, J.R., Wallace, S., Monaco, A.P., Barnby, G., Kobayashi, K., Lamb, J.A., Sousa, I., Sykes, N., Cook, E.H., Guter, S.J., Leventhal, B.L., Salt, J., Lord, C., Corsello, C., Hus, V., Weeks, D.E., Volkmar, F., Tauber, M., Fombonne, E., Shih, A., 2007. Mapping autism risk loci using genetic linkage and chromosomal rearrangements. Nat. Genet. 39, 319–328.

Talebizadeh, Z., Bittel, D.C., Veatch, O.J., Kibiryeva, N., Butler, M.G., 2005. Brief report: Non-random X chromosome inactivation in females with autism. J. Autism Dev. Disord. 35, 675–681.

Taniai, H., Nishiyama, T., Miyachi, T., Imaeda, M., Sumi, S., 2008. Genetic influences on the broad spectrum of autism: study of proband-ascertained twins. Am. J. Med. Genet. 147B, 844–849.

Tartaglia, N.R., Wilson, R., Miller, J.S., Rafalko, J., Cordeiro, L., Davis, S., Hessel, D., Ross, J. 2017. Autism Spectrum Disorder in Males with Sex Chromosome Aneuploidy: XXY/Klinefelter Syndrome, XYY, and XXYY. J. Dev. Behav. Pediatr 38, 197–207.

Tepest, R., Jacobi, E., Gawronski, A., Krug, B., MollerHartmann, W., Lehnhardt, F.G., Vogeley, K., 2010. Corpus callosum size in adults with high-functioning autism and the relevance of gender. Psychiatry Research: Neuroimaging 183, 38–43.

Tick, B., Bolton, P., Happé, F., Rutter, M. & Rijsdijk, F. (2016). Heritability of autism spectrum disorders: a meta-analysis of twin studies. J. Child Psychol. Psychiatry 57, 585–595.

Travers, B.G., Adluru, N., Ennis, C., Tromp, D.P.M., Destiche, D., Doran, S., Bigler, E.D., Lange, N., Lainhart, J.E., Alexander, A.L., 2012. Diffusion Tensor Imaging in Autism Spectrum Disorder: A Review. Autism Res. 5, 289–313.

Tsai, L.Y., Beisler, J.M., 1983. The development of sex differences in infantile autism. Br. J. Psychiatry 142, 373–378.

Tsakanikos, E., Underwood, L., Kravariti, E., Bouras, N., McCarthy, J., 2011. Gender differences in co-morbid psychopathology and clinical management in adults with autism spectrum disorders. Res. Autism Spectr. Disord. 5, 803-808.

Uljarevic, M. & Hamilton, A., 2013. Recognition of Emotions in Autism: A Formal Meta-Analysis. J. Autism Dev. Disord. 43, 1517–1526.

Van Wijngaarden-Cremers, P. J. M., van Eeten, E., Groen, W.B., Van Deurzen, P.A., Oosterling, I.J., Van der Gaag, R. J., 2014. Gender and age differences in the core triad of impairments in autism spectrum disorders: A systematic review and meta-analysis. J. Autism Dev. Disord. 44, 627–635.

Verdonk, P., Benschop, Y.W.M., de Haes, H.C.J.M. & Lagro-Janssen, T.L.M., 2009. From gender bias to gender awareness in medical education. Adv. in Health Sci. Educ. 14, 135-152.

Verma, D., Chakraborti, B., Karmakar, A., Bandyopadhyay, T., Singh, A.S., Sinha, S., Chatterjee, A., Ghosh, S., Mohanakumar, K.P., Mukhopadhyay, K., Rajamma, U., 2014. Sexual dimorphic effect in the genetic association of monoamine oxidase A (MAOA) markers with autism spectrum disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 50, 11–20.

Wakabayashi, A., Baron-Cohen, S., Uchiyama, T., Yoshida, Y., Kuroda, M., Wheelwright, S., 2007. Empathizing and systemizing in adults with and without autism spectrum conditions: cross-cultural stability. J. Autism Dev. Disord. 37, 1823–1832.

Wang, S., Deng, H., You, C., Chen, K., Li, J., Tang, C., Ceng, C., Zou, Y., Zou, X., 2017. Sex Differences in Diagnosis and Clinical Phenotypes of Chinese Children with Autism Spectrum Disorder. Neurosci. Bull. 33, 153–160.

Weigelt, S., Koldewyn, K. & Kanswisher, N. (2012). Face identity recognition in autism spectrum disorders: A review of behavioral studies. Neurosci. Biobehav. Rev. 36, 1060–1084.

Werling, D. M. & Geschwind, D. H., 2013. Sex differences in autism spectrum disorders. Curr Opin Neurol. 26, 146–153.

Werling, D.M., Lowe, J.K., Luo, R., Cantor, R.M., Geschwind, D.H., 2014. Replication of linkage at chromosome 20p13 and identification of suggestive sex-differential risk loci for autism spectrum disorder. Mol. Autism 5.

White, E.I., Wallace, G.L., Bascom, J., Armour, A.C., Register-Brown, K., Popal, H.S., Ratto, A.B., Martin, A., Kenworthy, L., 2017. Sex differences in parent-reported executive functioning and adaptive behavior in children and young adults with autism spectrum disorder. Autism Res. 10, 1653–1662.

Worley, J.A., Matson, J.L., 2011. Psychiatric symptoms in children diagnosed with an Autism Spectrum Disorder: An examination of gender differences. Res. Autism Spectr. Disord. 5, 1086–1091.

Yu, J., He, X., Yao, D., Li, Z., Li, H., Zhao, Z., 2011. A sex-specific association of common variants of neuroligin genes (NLGN3 and NLGN4X) with autism spectrum disorders in a Chinese Han cohort. Behav. Brain Funct. 7, 13.

Zeestraten, E.A., Gudbrandsen, M.C., Daly, E., De Schotten, M.T., Catani, M., Dell'Acqua, F., Lai, M.-., Ruigrok, A.N.V., Lombardo, M.V., Chakrabarti, B., Baron-Cohen, S., Ecker, C., Bailey, A.J., Baron-Cohen, S., Bolton, P.F., Bullmore, E.T., Carrington, S., Catani, M., Chakrabarti, B., Daly, E.M., Deoni, S.C.L., Ecker, C., Happé, F., Henty, J., Jezzard, P., Johnston, P., Jones, D.K., Lai, M.-., Lombardo, M.V., Madden, A., Mullins, D., Murphy, C.M., Murphy, D.G.M., Pasco, G., Ruigrok, A.N.V., Sadek, S.A., Spain, D., Stewart, R., Suckling, J., Wheelwright, S.J., Williams, S.C., Wilson, C.E., Murphy, D.G.M., Craig, M.C., 2017. Sex differences in frontal lobe connectivity in adults with autism spectrum conditions. Transl. Psychiatry 7.

Zhang, H.-F., Dai, Y.-C., Wu, J., Jia, M.-X., Zhang, J.-S., Shou, X.-J., Han, S.-P., Zhang, R. & Han, J.-S., 2016. Plasma oxytocin and arginine-vasopressin levels in children with Autism Spectrum Disorder in China: Associations with symptoms. Neurosci. Bull. 32, 423–432.

Supplementary data: Supplementary Tables 1-17.

Abbreviations used in all supplementary tables
AS = Asperger's syndrome
ASD = Autism spectrum disorder
HFA = high function autism
PDD = pervasive developmental disorder
F = female
M = male
NT = neurotypical

Other abbreviations are explained in under the table in which they are used.

Supplementary Table 1. Social communication and interaction.

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functi-oning of ASD particip ants**	**Results of measurements**	**ASD females compared to ASD males**
Backer van Ommeren 2017	ASD: 32 F, 114 M NT: 24 F, 55 M	6–18y	high and low	IDT social total: ASD F < NT F, p=.005, n^2=.15; ASD M < NT M, P<.001, n^2=.24; ASD F > ASD M, p<.05, n^2=.05	Social functioning ↑
Banach 2009	ASD: 48 F, 106 M	mean 9.3y	high and low	ADI social total and communication: F=M, p=n.s. VABS social and communication: F=M, p= n.s.	No differences
Baron-Cohen 2003a	ASD (AS/HFASD: 17 F, 51 M NT: 49 F, 27 M	mean 4.5y	high	FQ: ASD < NT, p<.001; NTF > NTM, p<.001; trend level difference ASD F> ASD M, P=.06	Friendship talents ↑
Bölte 2011	ASD: 21 F, 35 M	mean 14.4y	high	ADI-R social interaction and communication: F=M, p=n.s. ADOS social interaction and communication, F=M, p=n.s.	No differences
Carter 2007	ASD: 22 F, 68 M	1.5–2.8y	mainly low	ADI-R social interaction: trend level F>M, p<.10, n^2=.04 ADI-R communication: F=M, p=n.s. ADOS social interaction: F=M, p=n.s. ADOS communication: F>M, p<.05, n^2=.06 VABS communication: F>M, p<.05, n^2=.05	Social interaction and communication ↓
Coffman 2015	ASD: 12 F, 12 M	8.3–13y	high	ADI-R social affect: F=M, p=n.s. ADOS communication and interaction: F=M, p=n.s. VABS: communication and social: F=M, p=n.s.	No differences
Dean 2017	ASD: 24 F, 24 M NT: 24 F, 24 M	mean 7.7y	high	ADOS-2 social affect: F=M, p=n.s. POPE joint engagement: ASD F and NT F> ASD M and NT M, p=.006 POPE solitary: ASD group > NT group, p=.000; ASD M>ASD F, NT F, NT M, p=.03	Joint engagement ↑ Spending time with peers ↑
Dean 2014	ASD: 25 F, 25 M NT: 25 F, 25 M	6–10y	high	ADOS social communication: F=M, p= n.s. FS social acceptance, social connections, reciprocal friendship, group salience: ASD group < NT group, p<.001; ASD F= ASD M, p=n.s. FS rejection: ASD F, NT F< ASD M, NT M, p<.05	Social acceptance ↑
Grove 2017	ASD: 286 F, 265 M	mean 43.6y	high	AQ social behaviour scale F>M, p<.05	Social functioning ↓
Frazier 2014	ASD: 304 F, 2114 M	4–18y	high and low	ADI-R social interaction and communication: F=M, p= n.s. ADOS reciprocal social: F>M, p=.028, d=.09 ADOS communication: F>M, p=.013, d=.10 ADOS social affect: F>M, p=.029, d=.09 SRS social cognition: F>M, p=.028, d=.09 SRS social communication: F>M, p=.036, d=.09 SRS social awareness: F=M, p= n.s. SRS social motivation: F=M, p= n.s.	Social functioning ↓
Fulton 2017	ASD: 42 F, 177 M	2.4–6.2y	high and low	PLS communication: F=M, p=n.s.	No differences

Harrop 2015a	ASD: 40 F, 40 M	2.8–4.5y	?	ESCS: F=M, p=n.s.	No differences
Hartley 2009	ASD (133 A, 66 PDD-NOS): 42 F, 157 M	1.5–3.9y	mainly low	ADOS-G communication: F>M, p<.05 ADOS-G social interaction: F=M, p=n.s.	Communication ↓
Head 2014	ASD: 25 F, 25 M NT: 25 F, 26 M	10–16y	high	FQ: all F> all M, p<.05	Friendship talents ↑
Holtmann 2007	ASD: 23 F, 23 M	5–20y	high	ADI-R social interaction and communication: F=M, p=n.s. ADOS social interaction and communication: F=M, p=n.s.	No differences
Konstan-tareas 1989	ASD: 22 F, 67 M	2–18y	low	Imitation test: F<M, p=.02	Social imitation ↓
Kumazaki 2015	ASD: 20 F, 26 M	5–9y	high	CARS-TV relating to people, imitation, verbal and nonverbal communication: F=M, p=n.s.	No differences
Lai 2017b	ASD: 30 F, 30 M	18–49y, mean 27.5y	high	ADI-R social interaction: F=M, p=n.s. ADI-R communication: F<M, p=.029 ADOS communication: F<M, p<.001 Camouflage: F>M, p<.001	Social functioning ↑ Camouflage ↑
Lai 2013	ASD: 30 F, 30 M	mean 27.7y	high	ADI-R social interaction: F=M, p=n.s. ADI-R communication: F<M, p=.029 ADOS social interaction and communication F<M, p<.001	Social interaction and communication ↑
Lai 2012	ASD: 38 F, 45 M	18–49y	high	ADI-R social interaction and communication: F=M, p=n.s. ADOS social interaction and communication: F<M, p<.001	Social interaction and communication ↑
Lai 2011	ASD: 29 F, 33 M	18–45y	high	ADI-R social interaction and communication: F=M, p=n.s. ADOS social interaction: F<M, p=.015, d=.31 ADOS communication: F<M, p<.001, d=.48	Social interaction and communication ↑
Mandic-Maravic 2015	ASD: 25 F, 83 M	mean 6.7y	low	ADI-R social interaction and communication: F=M, p=n.s. VABS: F=M, p=n.s.	No differences
Mandy 2012	ASD: 52 F, 273 M	3–18y	high	3Di social interaction and communication: F=M, p=n.s. ADOS social interaction and communication: F=M, p=n.s. SDQ (teacher report) total: F<M, p=.01 SDQ (teacher report) prosocial behavior: F>M, p=.009 SDQ (teacher report) peer relationship problems: F<M, p=.05 SDQ (parent report) total: F=M, p=n.s.	Prosocial behavior ↑ Peer relationship ↑
May 2016	ASD: 32 F, 32 M NT: 30 F, 30 M	7–12y	high	CCC-2 total: ASD>NT, p<.015 CCC-2 inappropriate initiations F<M, p<.05 SRS total ASD>NT, p<.001, F=M, P=N.S.	Discussion talents ↑
Mussey 2017	ASD: 113 F, 566 M	1.8–56y	mainly low	ADOS-G communication and social interaction: F=M, p=n.s.	No differences
McLennan 1993	ASD: 21 F, 21 M	6–36y	high and low	ADI social interaction and communication total: F=M, p=n.s. ADI Deficits in social imitative play: F<M, p<.05	Imitative play ↑
Ormond 2018	ASD (54 A, 164 AS, 5 HFA, 13 PDD-NOS): 98 F, 138 M	5–19y	mainly high	Q-ASC social masking: F>M, p<.001, n^2=.07	Social masking ↑
Park 2012	ASD: 20 F, 91 M	mean 8.49y	high	ADI-R social interaction: F=M, p=n.s. ADI-R communication: F<M, p=.028 ASDS social: F=M, p=n.s.	Communication ↑
Pisula 2018	ASD: 21 F, 39 M NT: 1491 F, 1328 M	17–44y	high	AQ total: all F < all M, p<.001 AQ communication ASD F< ASD M, p<.05	Communication ↑
Postorino 2015	ASD: 30 F, 30 M	2.5–4y	mainly low	VABS communication and social skills: F=M, p=n.s.	No differences
Øien 2018	ASD: 23 F, 62 M NT: 12 F, 26 M	2.5–10y	high and low	AMSE eye contact, interest in others, pointing skills: ASD group > NT group, p<.001; F=M, p=n.s.	No differences
Reinhart 2015	ASD: 54 F, 234 M	1.5–2.8y	high and low	ADOS social affect: F=M, p=n.s. VABS communication and socialization: F=M, p=n.s. CSBS emotions, eye gaze and gestures: F=M, p=n.s	No differences
Rivet 2011	ASD: 66 F, 66 M NT: 66 F, 66 M	1.4–3y	?	BISCUIT: ASD group > NT group, p<.001, ASD F=ASD M, p=n.s.	No differences
	ASD: 37 F, 37 M NT: 37 F, 37 M	3–17y	low	ASD-DC nonverbal communication/socialization, verbal communication: ASD group > NT group, p<.001, ASD F=ASD M, p=n.s.	No differences

	ASD: 58 F, 58 M NT: 58 F, 58 M	adults	low	ASD-DA social impairment, communication impairment: ASD group > NT group, p<.001; ASD F=ASD M, p=n.s.	No differences
Rynkiewicz 2016	ASD: 10 F, 16 M	5–10y	high	Gesture using ASD F>ASD M (p values not told)	Gesture using ↑
Sedgewick 2016	ASD (19 A, 4 AS): 13 F, 10 M NT: 13 F, 10 M	12–16y	high and low	SRS-2 ASD F< ASD M, p=.02, d=1.03 SRS-2 NT F =NT M, p=n.s. FQ helping behaviour: ASD group < NT group, p=.03, n^2=.10; ASD F> ASD M, p=0.01, d=1.10 (other comparison n.s.) FQ closeness: ASD group < NT group, p=.01, n^2=.13, ASD F> ASD M, p=.01, n^2=.1.15 (other comparison n.s.) FQ security of friendship: all F > all M, p.001, n^2=.25 (other comparison n.s.) FQ conflicts: ASD group < NT group, p=.02, n^2=.11 (other comparison n.s.)	Social functioning ↑ Helping behaviour ↑ Friendship closeness ↑
Sipes 2011	ASD: 96 F, 294 M	1.4–3y	high and low	BISCUIT social F=M, p=n.s.	No differences
Solomon 2012	ASD: 20 F, 20 M NT: 19 F, 19 M	8–18y	high	ADOS-G communication and social: ASD F= ASD M, p=n.s. CCC-2: ASD group < NT group, p<.001; ASD F= ASD M, p=n.s. SCQ:ASD F= ASD M, p=n.s. SRS: ASD F= ASD M, p=n.s.	No differences
Supekar 2015	ASD: 25 F, 25 M	7–13y	high	ADI R social total and communication: ASD F = ASD M, p=n.s.	No differences
Szatmari 2012	ASD: 406 F, 1622 M	mean 8.5y	mainly high	ADI-R social total: F=M, p=n.s.	No differences
Tsai 1983	ASD: 23 F, 52 M	1.9–14.2y	low	DP-3 Social development: F<M, p<.05	Social development ↓
Wang 2017	ASD: 94 F, 373 M	2–6.9y	Non-verbal	ADI-R social reciprocity: F>M, p=.001,.38 ADI-R total communication: F=M, p=n.s. ADOS social reciprocity: F=M, p=n.s. ADOS communication F>M, p=.006, d=.32	Social reciprocity ↓ Social communication ↓
	ASD: 134 F, 463 M		verbal	ADI-R social reciprocity: F>M, p=-049, d=.22 ADI-R total communication: F=M, p=n.s. ADI-R gesture communication F>M, p<.001, d=.40 ADOS social reciprocity and communication: F=M, p=n.s.	Social reciprocity ↓
White 2017	ASD: 79 F, 158 M	7–18y	high and low	ADI social interaction and communication: F=M, p=n.s. ADOS-2 social interaction and communication: F=M, p=n.s. VABS communication: F=M, p=n.s.	No differences

ADOS = Autism Diagnostic Observation Schedule, ADI-R= Autism Diagnostic Interview-Revised, AMSE= Analysis of the Autism Mental Status Exam, ASD-DA= Autism Spectrum Disorders Diagnostic–Adult Version, ASD-DC= Autism Spectrum Disorders Diagnostic–Child Version, AQ= Autism Spectrum Quotient, BISCUIT= Baby and Infant Screen for Children with Autism Traits, CARS= Childhood Autism Rating Scale, CCC-2= Children's Communication Checklist–Second Edition, DP-3= Developmnetal Profile 3, ESCS= Early Social Communication Scales, FS=Friendships Survey, FQ=Friendship Questionnaire, FQS= Friendship Qualities Scale, FQS= Friendship Qualities Scale, IDT= Interactive Drawing Test, PLS= The Preschool Language Scale, POPE=Playground Observation of Peer Engagement, SCQ= Social Communication Questionnaires, SRS-2= Social Responsiveness Scale—2nd Edition VABS= Vineland Adaptive Behavior Scales

Supplementary Table 2. Repetitive and restricted behavior and interests (RRBIs).

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functi-oning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Banach 2009	ASD: 48 F, 106 M	mean 9.3y	high and low	ADI RRBI: F=M, p=n.s.	No differences
Bölte 2011	ASD (38 A, 11 AS, 7 PDD-NOS): 21 F, 35 M	mean 14.4y	high	ADI-R RRBI: F=M, p=n.s. ADOS: F<M, P=.02, n^2=.09	RRBI ↓
Carter 2007	ASD: 22 F, 68 M	1.5–2.8y	mainly low	ADI-R RRBI: F=M, p=n.s. ADOS RRBI: F=M, p=n.s.	No differences

Coffman 2015	ASD: 12 F, 12 M	8.3–13y	high	ADI RRBI: F<M, p<.05 ADOS RRBI: F=M, p=n.s.	RRBI ↓
Dean 2017	ASD: 24 F, 24 M	mean 7.7y	high	ADOS RRBI: F=M, p=n.s.	No differences
Dean 2014	ASD: 25 F, 25 M	6–10y	high	ADOS RRBI: F=M, p=n.s.	No differences
Frazier 2014	ASD: 304 F, 2114 M	4–18y	high and low	ADI-R RRBI total: F<M, p=.03, d=-.09 ADI-R repetitive sensory motor: F=M, p=n.s. ADI-R insistence on sameness: F=M, p=n.s. ADOS restrictive and repetitive: F=M, p=n.s. RBS-R total score: F=M, p=n.s. RBS-R stereotypy: F<M, trend level, p=.059, d=.08 RBS-R compulsive: F=M, p=n.s. RBS-R sameness: F=M, p=n.s. RBS-R restricted interests: F<M, p=.001, d=.13 SRS autism mannerisms: F=M, p=n.s.	RRBI ↓
Harrop 2015b	ASD: 29 F, 29 M	mean 3.1y	low	ADOS-2 RRBI: F=M, p=n.s. CCX RRBI total: F=M, p=n.s. CCX visual RRBI: trend level F<M, p=.05 RRBI was appositively associated with lower non-verbal abilities F (p=.03) and M, (p<.01)	Visual RRBI ↓
Hartley 2009	ASD (133 A, 66 PDD-NOS): 42 F, 157 M	1.5–3.9y	mainly low	ADOS-G RRBI: F<M, p<.05	RRBI ↓
Hattier 2011	ASD: 63 F, 77 M	20–78y mean 49.3y	low	DASH-II stereotypies: F<M, p=.019	Stereotypies ↓
Holtmann 2007	ASD: 23 F, 23 M	5–20y	high	ADI-R RRBI: F=M, p=n.s.	No differences
Joseph 2013	ASD: 20 F, 108 M NT: 15 F, 44 M	2–11y, mean 4.1y	?	RBS-R: ASD all > NT all (p not specified); ASD F= ASD M, p=n.s.	No differences
Kumazaki 2015	ASD: 20 F, 26 M	5–9y	high	CARS-TV body use, object use F<M, p<.05	Abnormalities in body and object use ↓
Lai 2017b	ASD: 30 F, 30 M	18–49y	high	ADI-R RRBI: F<M, p=.023 ADOS RRBI: F<M, p<.001	RRBI ↓
Lai 2013	ASD: 30 F, 30 M	mean 27.7y	high	ADI-R RRBI: F<M, p=.021 ADOS RRBI: F<M, p<.001	RRBI ↓
Lai 2012	ASD: 38 F, 45 M	18–49 y	high	ADI-R RRBI: F<M, p=.035 ADOS RRBI: F<M, p<.001	RRBI ↓
Lai 2011	ASD: 29 F, 33 M	18–45y	high	ADI-R RRBI: F<M, p=-048, d=-53 ADOS RRBI: F<M, p<.001, d=.50	RRBI ↓
Lord 1982	ASD: 91 F, 384 M	3–8y	low	CARS unusual visual interest: F < M, p<.001 PEP routinized and stereotypic play F<M, p<.05	Unusual visual interest ↓ Routinized and stereotypic play ↓
Mandic-Maravic 2015	ASD: 25 F, 83 M	mean 6.7y	low	ADI-R RRBI: F=M, p=n.s.	No differences
Mandy 2012	ASD: 52 F, 273 M	3–18y	high	3Di RRBI: F<M, p=.03 ADOS RRBI: F<M, p=.04 CCC large store of factual information: F<M, p=.006 CCC oddly formal play (e.g. ordering toys by size or colour) F<M, p=.026 CCC other dimensions F=M, p=n.s.	RRBI ↓ Stereotyped play ↓
May 2016	ASD: 32 F, 32 M NT: 30 F, 30 M	7–12y	high	CCC-2 total ASD>NT, p<.001 CCC-2 unusual interests F<M, p<.01 CCC-2 inappropriate initiation (e.g. talking repetitively even no one is interest) F<M, p<.05 RBQ total ASD>NT, p<.001 RBQ repetitive motor movements F<M, p<.01	Repetitive motor movements ↓ Unusual interest ↓ Repetitive talking ↓
McLennan 1993	ASD: 21 F, 21 M	6–36y, mean 14.4y	high and low	ADI RRBI: F=M, p=n.s.	No differences

Park 2012	ASD: 20 F, 91 M NT: 25 F, 26 M, Siblings of ASD participants: 51 F, 47 M	mean 8.5y	high	ADI-R RRBI: ASD group > NT group; unaffected siblings F< unaffected siblings M, p<.001; ASD F< ASD M, p=.045	RRBI ↓
Postorino 2015	ASD: 30 F, 30 M	2.5–4y	mainly low	ADOS-G RRBI: F=M, p=n.s.	No differences
Øien 2018	ASD: 23 F, 62 M	2.5–10y	high and low	AMSE RRBI: F=M, p=n.s.	No differences
Reinhart 2015	ASD: 54 F, 234 M	1.5–2.8y	high and low	ADOS RRBI: F=M, p=n.s.	No differences
Rivet 2011	ASD: 66 F, 66 M NT: 66 F, 66 M	1.4–3y	?	BISCUIT: ASD group > NT group, p<.001, ASD F=ASD M, p=n.s.	No differences
	ASD: 37 F, 37 M NT: 37 F, 37 M	3–17y	low	ASD-DC insistence of sameness/restricted interest: ASD group > NT group, p<.001, ASD F=ASD M, p=n.s.	No differences
	ASD: 58 F, 58 M NT: 58 F, 58 M	adults	low	ASD-DA: restricted interest: ASD group > NT group, p<.001, ASD F=ASD M, p=n.s.	No differences
Sipes 2011	ASD: 70 F, 221 M	1.4–3y	low	BISCUIT RRBI: ASD F = ASD M	No differences
	ASD: 26 F, 73 M		high	BISCUIT RRBI: ASD F < ASD M (difference is significant, but p values not given)	RRBI ↓
Solomon 2012	ASD: 20 F, 20 M NT: 19 F, 19 M	8–18y	high	RBS-R: ASD group > NT group, p<.001 RBS-R restricted interests: ASD F< ASD M, p=.015	Restricted interest ↓
Supekar 2015	ASD: 25 F, 25 M	7–13y	high	ADI-R RRBI: ASD F<ASD M, p<.01	RRBI ↓
Szatmari 2012	ASD: 406 F, 1622 M	mean 8.5y	mainly high	ADI-R RRBI: F<M, p<.0001	RRBI ↓
Wang 2017	ASD: 94 F, 373 M	2–6.9y	nonverbal	ADI-R RRBI: F<M, p<.001, d=.13 ADI R hand and finger mannerisms: F>M, p=.003 ADI-R unusual preoccupation, repetitive use of objects, interest parts of objects: F<M, p<.05 ADOS RRBI: F<M, p=.006, d=.32	RRBI total ↓ Repetitive use of objects ↓ Interests parts of objects ↓ Unusual preoccupation ↓ Hand and finger mannerism ↑
	ASD: 134 F, 463 M		verbal	ADI-R RRBI: F<M, p<.001, d=.32 ADI-R repetitive speech: F<M, p=.003, d=.29 ADI-R unusual preoccupation, repetitive use of objects, circumscribed interests, interest parts of objects: F<M, p<.05 ADOS RRBI: F<M, p=.006, d=.13	RBB total ↓ Repetitive speech ↓ Repetitive use of objects ↓ Interests parts of objects ↓ Unusual preoccupation ↓ Circumscribed interest ↓
White 2017	ASD: 79 F, 158 M	7–18y	high and low	ADI-R RBB: F=M, p=n.s. ADOS-2 RRBI: F=M, p=n.s.	No differences

3Di=The Develop-mental, Dimensional and Diagnostic Interview, ADOS = Autism Diagnostic Observation Schedule, ADI-R= Autism Diagnostic Interview-Revised, ASD-DA= Autism Spectrum Disorders Diagnostic–Adult Version, ASD-DC= Autism Spectrum Disorders Diagnostic–Child Version, BISCUIT= Baby and Infant Screen for Children with Autism Traits, CARS= Childhood Autism Rating Scale, CCC= Children's Communication Checklist, CCX= a videotaped caregiver–child interaction, DASH-II= Diagnostic Assessment for the Severely Handicapped-Second Edition, PEP= Psychoeducational Profile, RBS-R= Repetitive Behavior Scale–Revised, SRS= Social Responsiveness Scale

Supplementary Table 3. Sensory symptoms.

Article (first author and year)	**Participants**			**Results**	
	Number of ASD participants	**Age**	**Functioning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Amr 2011	23 F, 37 M	4–11y, mean 8.2y	high and low	ISAA sensory aspects, F>M, p=.05	Sensory aspects ↑
Kumazaki 2015	26 F, 20 M	5–9y	high	CARS-TV taste, smell, touch response and use: F>M, p<.01	Abnormal taste, smell, touch response and use ↑
Mandy 2012	52 F, 273 M	3–18y	high	3Di auditory sensitivity: F = M	No difference
Lai 2011	29 F, 33 M	18–45 y	high	ADI-R unusual sensory response F>M, p=.036	Unusual sensory responses ↑
Øien	23 F, 62 M	2.5–10y,	high and	AMSE unusual sensitivities F<M,	Unusual sensitives ↓

2018		mean 5.7y	low	p<.05	
Ormond 2018	98 F, 138 M	5–19y	high	Q-ASC sensory sensitivity F>M, p=<.001, n^2=.05	Sensory sensitivity ↑
Park 2012	20 F 91 M	mean 8.5y	high	ASDS sensory motor F = M	No difference

ADI -R= Autism Diagnostic Interview-Revised, AMSE= Analysis of the Autism Mental Status Exam, CARS= Childhood Autism Rating Scale, ISAA= Indian Scale for Assessment of Autism, Q-ASC= The Questionnaire for Autism Spectrum Conditions

Supplementary Table 4. Cognitive ability.

Article	**Participants**		**Methods**	**Variables**		**Comparison between ASD female and ASD male**	
	Number of ASD participants	**Age**		**Females mean (SD)**	**Males mean (SD)**		
Ankeman 2014	244 F, 1710 M	4–17y	DAS-II	NVIQ:88.19 (20.43) VIQ: 88.22 (23.32)	NVIQ: 93.75 (18.67) VIQ: 89.61 (21.50)	NVIQ: F<M, p<.001 VIQ: F=M, n.s.	NVIQ ↓
Backer van Ommeren 2017	32 F, 114 M	6–18y	PPVT	VIQ=99.7 (11.2)	VIQ=105.5 (14.2)	VIQ: F<M, p<.05, n^2=.03	VIQ↓
Banach 2009	MX: 45 F, 95 M SPX: 45 F, 195 M	mean 9.3y	Leiter	MPX: IQ:74.76 (30.36) SPX: IQ: 50.21 (22.80)	MPX: IQ: 68.87 (31.83) SPX: IQ: 76.15 (29.45)	MPX IQ: F=M, n.s. SPX: F<M, p<.001	MPX: No differences SPX: IQ ↓
Bölte 2011	21 F, 35 M	mean 14.4y	WISC-R /Raven	NVIQ: 98.6 (9.8)	NVIQ: 99.8 (11.3)	NVIQ: F=M, n.s.	No differences
Frazier 2014	304 F, 2114 M	4–18y	WISC, WASI	IQ: 74.70 (27.59) NVIQ: 77.40 (26.17) VIQ: 73.43 (31.95) VIQ–NVIQ: -3.97 (16.34)	IQ: 82.56 (27.59) NVIQ:85.96 (25.81) VIQ: 79.16 (30.74) VIQ–NVIQ: -6.79 (17.04)	IQ: F<M, p<.001, d=.19 NVIQ: F<M, p<.001, d=.22 VIQ: F<M, p=.003, d=.12 VIQ–NVIQ: F<M, p<.007, d=.11	IQ ↓ NVIQ ↓ VIQ ↓ VIQ-NVIQ ↓
Fulton 2017	42 F, 177 M	2.4–6.2y	MSEL	IQ: 52.27 (18.04)	IQ: 51.54 (21.14)	IQ: F=M, n.s.	No differences
Kumazaki 2015	20 F, 26 M	59y	WISC-III	IQ: 97.5 (13.6) NVIQ: 98.3 (12.7) VIQ: 97.3 (15.2)	IQ: 97.6 (13.5) NVIQ: 98.5 (11.3) VIQ: 96.9 (11.3)	IQ: F=M, n.s. NVIQ: F=M, n.s. VIQ: F=M, n.s.	No differences
Lehnhardt 2016	38 F, 69 M	Adults	WAIS-III	IQ: 110.2 (14.4) NVIQ: 108.3 (15.6) VIQ: 110.0 (13.0) VIQ–NVIQ: 1.7 (11.6)	IQ: 111.7 (13.9) NVIQ: 106.2 (15.9) VIQ:114.7 (12.9) VIQ–NVIQ: 8.5 (13.9)	IQ: F=M, n.s. NVIQ: F=M, n.s. VIQ: F=M, n.s. VIQ–NVIQ: F<M, p<.001	IQ: No differences VIQ-NVIQ ↓
Lord 1982	91 F, 384 M	3–8y,	Bayley / WISC-R /Leiter /Merrill-Palmer Scale	NVIQ: 37.23 (16.88)	NVIQ: 43.62 (20.24)	NVIQ: F<M, p<.05	NVIQ↓
May 2016	32 F, 32 M	7–12y,	WISC-IV, WPPSI	IQ: 96.19 (21.50) NVIQ: 97.12 (14.09) VIQ: 99.12 (13.42)	IQ: 97.38 (13.86) NVIQ:104.84 (15.10) VIQ: 98.66 (14.34)	IQ: F=M, n.s. NVIQ: F=M, n.s. VIQ: F=M, n.s.	No differences
Mussey 2017	113 F, 566 M	1.8y–56y	Wechsler scales or equivalent (not specified)	IQ: 85.59 (22.1) NVIQ: 89.65 (20.8) VIQ:90.68 (21.4)	IQ: 85.98 (21.8) NVIQ: 94.74 (19.8) VIQ: 92.27 (20.8)	IQ: F=M, n.s. NVIQ: F=M, n.s. VIQ: F=M, n.s.	No differences
Reinhart 2015	54 F, 234 M	mean 2.3y	MSEL	NVDQ: 82.98 (25.91) VDQ: 71.82 (32.02)	NVDQ: 82.49 (23.76) VDQ70-05 (28.78)	NVDQ: F=M, p=n.s. VDQ: F=M, p=n.s.	No differences
Tsai 1983	23 F, 52 M	1.9y – 14.3y	Wechsler scales or	IQ: 42.13 (26.78)	IQ:57.38 (15.52)	IQ: F<M, p=.025	IQ ↓

			equivalent				

MPX= multiplex ASD child families, SPX: simplex ASD child families DASH-II= Diagnostic Assessment for the Severely Handicapped-Second Edition, IQ=Intelligent quotient, MSEL= Mullen Scales of Early Learning, NVDQ nonverbal developmental quotient, NIVQ= Nonverbal Intelligent quotient, PPVT= Peabody Picture Vocabulary Test, VDQ verbal developmental quotient VIQ=Verbal Intelligent quotient WAIS= Wechsler Adult Intelligence Scale, WISC= The Wechsler Intelligence Scale for Children, WPPSI-III= Wechsler Preschool and Primary Scale of Intelligence

Supplementary Table 5. Language functions.

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functi-oning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Backer van Ommeren 2017	ASD: 32 F, 114 M NT: 24 F, 55 M	6 –18y	high and low	PPVT-R: F<M, p<.05, n^2=.03	Language abilities ↓
Carter 2007	ASD: 22 F, 68 M	1.5–2.8y	mainly low	MSEL receptive language: F=M, p=n.s. MSEL expressive language: F=M, p=n.s.	No differences
Frazier 2014	ASD: 304 F, 2114 M	4–18y	high and low	CTOPP non-word repetition: F<M, p=.005, d=.13 PPVT-R: F<M, p<001, d=22	Vocabularity ↓ Non-word repetition ↓
Goddard 2014	ASD: 12 F, 12 M NT: 12 F, 12 M	8–16y	high	Verbal fluency: ASD and NT F>ASD and NT M, p=.03, n^2=.65	Verbal fluency ↑
Hartley 2009	ASD (133 A, 66 PDD-NOS): 42 F, 157 M	1.5–3.9y	mainly low	MSEL receptive language: F=M, p=n.s. MSEL expressive language: F=M, p=n.s.	No differences
Kiep 2017	ASD: 40 F, 99 M NT: 25 F, 35 M	mean 37.1y	high	Verbal fluency (K letter): ASD F<ASD M, p=.023, n^2=.052; ASD F= NT F, p=n.s.; ASD M< NT M, p=.003, n^2=.164 Verbal fluency (M letter): ASD F= ASD M, p=n.s; ASD F= NT F, p=n.s.; ASD M= NT M, p=n.s. Verbal fluency (semantic, animals): ASD F> ASD M, p=.007, n^2=.162; ASD F= NT F, p=n.s.; ASD M<NT M, p.001, n^2=.190 Verbal fluency (semantic, professions): ASD F= ASD M, p=n.s.; ASD F= NT F, p=n.s.; ASD M<NT M, p=.002, n^2=.173	Phonemic verbal fluency ↓ Semantic verbal fluency ↑
Konstan-tareas 1989	ASD: 22 F, 67 M	2–18y	low	PPVT-R receptive language: F<M trend level, p=.06 PPVT-R expressive language: F=M, p=n.s.	Receptive language ↓
Lai 2012	ASD: 38 F, 45 M NT: 35 F, 33 M	18–49y	high	Non-Word Repetition: ASD group = NT group, p=n.s.; F=M, p=n.s. Word generativity (F-A-S): ASD group = NT group, p=n.s. All F> All M, p=.012	Word generativity ↑
Lehnhart 2016	ASD: 38 F, 69 M	adults	high	Verbal fluency (letter): F>M, p=.007 Verbal fluency (semantic): F>M, p=.034	Verbal fluency ↑
Øien 2018	ASD: 23 F, 62 M	2.5–10y	high and low	AMSE language F<M, p<.05	Language abilities ↓
Reinhart 2015	ASD: 54 F, 234 M	1.5–2.8y	high and low	CSBC word: F<M, p<.05 CSBC other dimensions F=M, p=n.s.	Language abilities ↓
Ross 2015	ASD: 15 F, 58 M NT: 47 F, 55 M	5–17y	high	Multisensory speech processing task, word recognition: All F>All M, p<.05 ASD F>ASD M, p<.05	Word recognition ↑
Scheider 2013	ASD: 13 F, 15 M NT: 13 F, 15 M	18–55y	high	Verbal fluency (lexical): ASD group = NT group, p=n.s.; ASD F=ASD M, p=n.s. Verbal fluency (semantic): ASD group = NT group, p=n.s.; ASD F> ASD M, p=.03	Semantic verbal fluency ↑

AMSE= Analysis of the Autism Mental Status Exam, CSBS= Communication and Symbolic Behavior Scales Developmental Profile, CTOPP= Comprehensive Test of Phonological Processing, PPVT= Peabody Picture Vocabulary Tes

Supplementary Table 6. Executive functions.

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functioning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Bölte 2011	ASD: 21 F, 35 M Siblings of ASD participants 35 F, 23 M	mean 14.4y	high	Block Design: ASD F< ASD M, p=.02, n^2=.05 TMT B-A: ASD F>ASD M, p=.04, n^2=.04 ToH: ASD group = NT group, p=n.s.; ASD F= ASD M, p=n.s. WCST: ASD group < NT grop, p<.05; ASD F= ASD M, p=n.s. EFT: ASD group = NT group, p=n.s.; ASD F= ASD M, p=n.s.	Cognitive flexibility ↑ Visuospatial ability ↓
Kiep 2017	ASD: 40 F, 99 M NT: 25 F, 35 M	mean 37.1y	high	ToH: ASD F = ASD M, p=n.s; ASD group = NT group, p=n.s. WAIS-III working memory: ASD F>ASD M, p<.005, n^2=.291, ASD F<NT F, p=.009, n^2=.222; ASD M<NT M, p<.005, n^2=.387 WCST non-perseverative errors: ASD F< ASD M, p=.004, n^2=.175; ASD F=NT F, p=n.s.; ASD M>NT M, p=.014, n^2=.13 WCST perseverative errors: ASD F>ASD M, p=.029, n^2=.124; ASD F> NT F, p=.05, n^2=.155; ASD M> NT M, p=.014, n^2=.13	Cognitive flexibility ↓ Working memory ↑
Kumazaki 2015	ASD: 26 F, 20 M	5-9y	high	Block Design: F=M, p=n.s. Digit symbol coding: F>M, trend level p=.07	Processing speed ↑
Lai 2017b	ASD: 30 F, 30 M	18–49y, mean 27.5y	high	Go/No Go task: F=M, p=n.s.	No differences
Lai 2012	ASD: 38 F, 45 M NT: 35 F, 33 M	18–49 y	high	Go/No Go task: ASD < NT, p<.001; ASD F= ASD M, p=n.s. EFT: ASD F=NT F, p=n.s.; ASD M<NT M, P<.05	Central coherence ↑
Lehnhardt 2016	ASD: 38 F, 69 M	adults	high	Digit symbol coding: F>M, p=.007 TMT A: F<M, p=.004 TMT B: F=M, p=n.s. WCST: F=M, p=n.s.	Processing speed ↑
Lemon 2011	ASD: 13 F, 10 M NT: 14 F, 8 M	6–16y	high	Stop task reaction time: ASD F> ASD M, p=.025, d=.86 ASD F> NT F, p=.002, d=1.30	Increased stopping time; indicate poorer inhibition ↓
Memari 2013	ASD: 29 F, 94 M	7–14y	high	WCST perseverative errors F>M, p=.012 WCST categories completed F<M, p=.002	Cognitive flexibility ↓
White 2017	ASD: 79 F, 158 M	7–18y	high and low	BRIEF executive function problems total F>M, p=.03, n^2=.02	Executive functions ↓

BRIEF= Behavior Rating Inventory of Executive Function, EFT= embedded figure test, TMT= Trail Making Test, TOH=Tower of Hanoi, WCST = Wisconsin Card Sorting Test

Supplementary Table 7. Emotion and face recognition.

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functioning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Baron-Cohen 2015	ASD: 217 F, 178 M NT: 168 F, 152 M	mean 39.2y	?	RMET: NT F > NT M, p<.001, n^2=.47; ASD F=ASD M, p= n.s.; ASD F < NT F, p<.001, n^2=.69ASD M< NT M, p<.001, n^2=.35	No differences
Coffman 2015	ASD: 12 F, 12 M	8.3–14y	high	Benton face recognition test: F=M, p=n.s.	No differences
Lai 2017b	ASD: 30 F, 30 M	18–49y mean 27.5y	high	RMET: F=M, p=n.s.	No differences

Lai 2012	ASD: 38 F, 45 M	18–49y	high	KDEF total: ASD group < NT group, p≤.001, All F > all M, p values depending emotion <.001-.058, ASD F> ASD M, p values depending emotion <.001-.028 RMET: ASD group < NT group, p<.001, F=M, p=n.s.	Emotion recognition ↑
Lehnhardt 2016	ASD: 38 F, 69 M	adults	high	RMET: F=M, p=n.s.	No differences
Rynkiewicz 2016	ASD: 10 F, 16 M	5–10y	high	Face Test: emotion recognition: ASD F<ASD M, (significant difference but p value not told)	Emotion recognition ↓
Scheider 2013	ASD: 13 F, 15 M NT: 13 F, 15 M	18–55y	high	PERT40 emotion recognition: ASD F=ASD M, p=n.s.	No differences
Sucksmith 2013	ASD: 150 F, 160 M NT: 96 F, 92 M Parents of ASD child: 261 F, 36 M	adults	high	KDEF performance: ASD group < NT, p<.001; All F > all M, p<.001; ASD F> ASD M, p<.001	Emotion recognition ↑

KDEF= Karolinska directed emotional faces task, RMET= The Reading the Mind in the Eyes Test,

Supplementary Table 8. Empathizing and systemizing.

Article (first author and year)	**Participants**			**Results**	
	Number of participants	**Age**	**Functioning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males**
Auyeung 2009	ASD (196 AS/HFA): 46 F, 219 M NT: 675 F, 581 M	4–11y	mostly high	EQ-C: ASD F= ASD M, p=n.s.; ASD all < NT M < NT F, p<.001 SQ-C: ASD all> NT M>NT F, p <.001; ASD F= ASD M, p=n.s.	No differences
Baron-Cohen 2003b	ASD (AS/HFA): 14 F, 33 M NT: 164 F, 114 M	mean 34.5y	high	EQ: ASD all < NT all, p<.0001; NT F> NT M, p<.0001; ASD F= ASD M, p=n.s. SQ: ASD all> NT all, p =.03; NT F < NT M, P<.0001; ASD F= ASD M, p=n.s.	No differences
Baron-Cohen 2014	ASD (506 AS, 41 HFA, 11 A, 15 PDD-NOS): 454 F, 357 M NT: 2562 F, 1344 M	mean 34.5y	?	EQ: ASD all < NT all, p <.001; NT F> NT M, p <.001, d=.76; ASD F> ASD M, p <.001, d=.40 SQ-R: ASD all> NT all, p <.001; NT F < NT M, p <.001, d=.61; ASD F< ASD M, p <.001, d=.27	EQ ↑ SQ ↓
Lai 2011	ASD: 29 F, 33 M	18–45y	high	SQ-R: ASD F= ASD M, p=n.s. EQ: ASD F= ASD M, p=n.s.	No differences
Lehnhardt 2016	ASD: 38 F, 69 M	adults	high	SQ-R: ASD F= ASD M, p=n.s. EQ: ASD F= ASD M, p=n.s.	No differences
Park 2012	ASD: 20 F, 91 M NT: 25 F, 26 M Siblings of ASD participants: 51 F, 47 M	mean 8.5y	high	EQ-C: ASD F= ASD M, p=n.s.; NT F =NT M, p=n.s.; Siblings F > siblings M, p<.001 SQ-C: ASD F= ASD M, p=n.s.; NT F < NT M, p=.016; Siblings F > siblings M, p=n.s.	No differences
Schwarz 2011	ASD (45 AS): 22 F, 23 M NT: 26 F, 24 M	mean 31.7y	high	EQ: ASD F <ASD M < NT M < NT F, p<.05 SQ: ASD F > NT M =ASD M > NT F, p<.05	EQ ↓ SQ ↑
Wakabayashi 2007	ASD: 10 F, 38 M NT: 700 F, 687 M	16–48y	high	EQ: ASD all < NT all, p<.001; NT F> NT M, p<.001; ASD F= ASD M, p=n.s. SQ: ASD all> NT all, p<.001; NT F < NT M, p<.001; ASD F= ASD M, p=n.s.	No differences

EQ= Empathy Quotient, EQ-C= Empathy Quotient Children, SQ= Systemizing Quotient, SQ-R= Systemizing Quotient-Revised, SQ-C= Systemizing Quotient Children

Supplementary Table 9. Psychiatric and neuropsychiatric comorbid diagnosis and symptoms.

Article (first author and year)	**Participants**			**Results**	
	Numer of participants	**Age**	**Functi-oning of ASD participants**	**Results of measurements**	**ASD females compared to ASD males or NT females**

Amr 2012	ASD: 23 F, 37 M	6–11y	low	SCICA anxiety, ADHD, depression, conduct disorder, any psychiatric disorders: F=M, n.s	No differences
Amr 2011	ASD: 23 F, 37 M	4–11y, mean 8.2y	high and low	CBCL attention problems, thought problems, aggressive behavior, internalizing, externalizing, total problems: F=M, n.s CBCL delinquent behavior F<M, p=0.018 CBCL anxiety/depression, F>M trend level p=.6 CBCL social problems F<M, trend level, p=.6	Delinquent behavior ↓ Anxiety ↑ Depression ↑ Social problems ↓
Baghdali 2003	ASD: 36 F, 164 M	2–7y	mainly low	Self-injury behavior: F=M, p=n.s., but females are overrepresented in group that have self-injurious	No differences
Cohen 2010	ASD: 60 F, 206 M NT: 854 F, 1152 M	6–65y, mean 41.7y	high and low	IBR self-directed aggression: ASD group > NT group, p<.001 (stronger effect ASD females than ASD males) IBR self-directed verbal aggression ASD F> ASD M, NT group, p=.044	Self-directed aggression ↑
Duerden 2010	ASD: 38 F, 212 M	2.3–19y, mean 7.3y	high and low	RBS-R self-injury: F=M, p=n.s.	No differences
Frazier 2014	ASD: 304 F, 2114 M	4–18y	high and low	CBCL total problems: F>M, p=.008, d=.11 CBCL internalizing: F=M, p=n.s. CBCL externalizing: F>M, p=.010, d=.10 ABC total: F=M, p=n.s. ABC irritability: F>M, p<.001, d=.15 ABC lethargy: F>M, p=.001, d=.14 ABC Hyperactivity: F=M, p=n.s. RBS-R Self-Injury: F>M, p=.044, d=.09	Externalizing ↑ Irritability ↑ Lethargy ↑ Self-injury ↑ Total problems ↑
Gadow 2012	ASD (45 A, 32 AS, 70 PDD-NOS): 17 F, 102 M	6–12y, mean 8.7y	high and low	CASI-4R schizophrenia spectrum traits (mothers rating) F>M, p=.005 CASI-4R schizophrenia spectrum traits (teacher rating) F=M, p=n.s.	Schizophrenia spectrum traits ↑
Hartley 2009	ASD (133 A, 66 PDD-NOS): 42 F, 157 M	1.5–3.9y	mainly low	CBCL internalizing, externalizing, emotionally reactive, somatic complaints, withdrawn, attention, aggression, total problems: F=M, p=n.s. CBCL anxiety, depression: F>M, p<.05 CBCL sleep problems: F>M, p<.05	Anxiety ↑ Depression ↑ Sleep problems ↑
Holtmann 2007	ASD: 23 F, 23 M	5–20y	high	CBCL somatic complains, anxiety, depression, delinquent behavior, aggression, F=M, p=n.s. CBCL total problems: F>M, p=.02, d=.80 CBCL social withdrawal: trend levels F>M, p=.06, d=.53 CBCL social problems: F>M, p<.01, d= 1.20 CBCL though problems: F>M, p<.01, d=.84 CBCL attention problems: F>M, p<.01, d=.80	Social withdrawal ↑ Social problems ↑ Though problems ↑ Attention problems ↑ Psychiatric problems ↑
Kaartinen 2014	ASD (7 A, 86atypical autism, 22 AS): 8 F, 27 M NT: 8 F, 27 M	7–17y	high	PAM reactive impulsive aggression: ASD F< NT F, p=.039; ASD M > NT M, p=.013 PAM reactive controlled aggression: ASD F= NT F, p=n.s.; ASD M> NT M, p=.040	Reactive aggression ↓ (comparison NT F)
Kozlowski 2012	ASD: 75 F, 92 M NT: 112 F, 112 M	2–17y, mean 8.1y	?	ASD-BPC challenging behaviour: ASD group>NT group, p<.05, ASD F=ASD M, p=n.s.	No differences
Lai 2017b	ASD: 30 F, 30 M	18–49y, mean 27.5y	high	BAI: F=M, p=n.s. BDI: F=M, p=n.s.	No differences
Lai 2011	ASD: 29 F, 33 M	18–45 y	high	BAI: F=M, p=n.s. BDI: F=M, p=n.s. OCI-R: F=M, p=n.s.	No differences
Magiati 2016	ASD (221 A, 15 AS, 5 PDD-NOS): 44 F, 197 M	6–18y, mean 10.3y	high and low	SCAS-P anxiety: F=M, p=n.s. repetitive behaviour symptoms was associated with anxiety p<.001	No differences
Mandy 2012	ASD (113 A, 94 AS, 118 PDD-NOS): 52 F, 273 M	3–18y	high	SDQ (parent report) total: F=M, p=n.s. SDQ (parent report) emotional symptoms: F>M, p=.02 SDQ (teacher report) total: F<M, p=.01	Emotional symptoms ↑ Hyperactivity ↓ Inattention ↓

				SDQ (teacher report) hyperactivity/inattention: F<M, p<.001	Psychiatric problems ↓
May 2016	ASD: 32 F, 32 M NT: 30 F, 30 M	7–12y	high	Conners 3 inattention: ASD>NT, p<.001, F=M, p=n.s. Conners 3 hyperactivity: ASD>NT, p<.001, F<M, p<.01 SWAN inattention: ASD>NT, p<.001, F<M, p<.05 SWAN hyperactivity: ASD>NT, p<.001, F<M, p<.05	Hyperactivity ↓ Inattention ↓
Mayes 2013	ASD (651 HFA, 382 LFA): 172 F, 861 M	1–16y	high and low	CASD unusual phobias: ASD F>ASD M, p=.02	Unusual phobias ↑
Oswald 2016	ASD: 14 F, 18 M NT: 14 F, 18 M	12–18y, mean 14.8y	high	RCADS-P anxiety: ASD group > NT group, p<.001, n^2=.28 RCADS-P depression: ASD group > NT group, p<.001, n^2=.32; early adolescence ASD F>ASD M, NT F, p=.001 MASC anxiety: ASD group > NT group, p<.005, n^2=.09 MASC depression: ASD group > NT group, p<.01, n^2=.12; ASD F> ASD M, NT F, p<.05	Depression ↑
Pisula 2017	ASD: 35 F, 35 M NT: 24 F, 24 M	11 –18y	high	CBCL attention problems, thought problems, aggressive behavior, internalizing, externalizing, somatic complains, delinquent behavior, withdrawn, total problems: ASD group > NT group, p<.001; ASD F=ASD M, p=n.s. YSR withdrawn, thought problems, social problems, internalizing: ASD group > NT group, p<.001; ASD F=ASD M, p=n.s. YSR anxiety, depression attention problems, aggressive behavior, externalizing, somatic complains, delinquent behavior, total problems: ASD group = NT group, p=n.s.; ASD F=ASD M, p=n.s.	No differences
Pohl 2014	ASD: 415 F, NT: 415 F	24–52y	mainly high	TMQ anorexia: ASD F>NT F, p=.000	Anorexia ↑ (comparison NT F)
Postorino 2015	ASD: 30 F, 30 M	2.5–4y	mainly low	CBCL anxiety, depression, internalizing, externalizing, emotionally reactive, somatic complaints, withdrawn, attention, aggression, total problems F=M, p=n.s. CBCL sleep problems F<M, p=.047	Sleep problems ↓
Simonoff 2008	ASD: 14 F, 98 M	10–14y	?	CAPA any psychiatric disorder: ASD F = ASD M, p=n.s. (69% M, 76% F) Any neuropsychiatric disorder: ASD F = ASD M, p=n.s. (29% M, 17% F)	No differences
Solomon 2012	ASD: 20 F, 20 M NT: 19 F, 17 M	8–18y	high	BASC2 anxiety, depression and internalizing: ASD F > ASD M, NT F > NT M, p<.001 CDI: ASD F> NT F, p<.001 (other p values not told)	Anxiety ↑ Depression ↑ Internalizing ↑
Tsakanios 2011	ASD: 50 F, 100 M	16–84y, mean 28.5y	low	Data collection from medical records: Psychiatric diagnosis: F<M, p<.01 Personality disorders: F<M, p<.05 Schizophrenia spectrum disorders: F<M, <.05 Anxiety, depression: F=M; p=n.s.	Personality disorders ↓ Schizophrenia spectrum disorders ↓ Psychiatric diagnosis ↓
Worley 2011	ASD: 26 F, 44 M NT: 32 F, 27 M	4–16y	high	ASD-CC tantrum behavior, worry/depressed, avoidant behavior, under-eating, conduct behavior, over eating: ASD group > NT group, p<.001; ASD F = ASD M, p=n.s.	No differences

ABC= Aberrant Behavior Checklist, ASD-BPC=Autism Spectrum Disorder-Behavior Problems for Children, CBCL= Child Behavior Checklist, BANI-Y= The Beck Anger Inventory for Youth, BASC2= Behavior Assessment System for Children-2nd Edition, CAPA= The Child and Adolescent Psychiatric Assessment-parent version, CASD= Checklist for Autism Spectrum disorder, IBR= IBR Modified Overt Aggression Scale, MASC= The Multidimensional Anxiety Scale for Children, PAM=Pulkkinen Aggression Machine, RADS-2= Reynolds Adolescent Depression Scale, RBS-R= Repetitive Behavior Scale–Revised, RCADS-P=The Revised Child Anxiety and Depression Scale—Parent Version, SCAS= Spence Children's Anxiety ScaleSCAS-P= Spence Children's Anxiety Scale–Parent Version, SCICA= The semi-structured clinical interview for children and adolescents, SWAN= Strengths and Weaknesses of Attention-Deficit /Hyperactivity-symptoms and Normal-behaviors, YSR=Youth self-report

Supplementary Table 10. Epilepsy and minor neurological deficits.

Article (first author and year)	**Participants**			**Methods**	**Results**		
	Number of ASD participants	**Age**	**Functioning of ASD participants**		**Results of measurement**	**ASD females compared to NT females**	**ASD females compared to ASD males**
Ben-Itzchak 2013	86 F, 577 M	1.5 – 15y	high and low	Neuro-logical examination	Seizures: ASD F>ASD M, trend level, p<-01 Minor neurological deficits (e.g hyperflaxity of joints, hypotonia, abnormal tendon reflex): ASD F>ASD M, p<.001 Macrocephaly: ASD group > references, p<.001; ASD F=ASD M, p=n.s. Microcephaly: ASD F> NT F references, p<.00; ASD M>NT M references, p<.05; ASD F>ASD M (F 15.1%, M 4.5%, p<.001)	Microcephaly ↑ Macrocephaly ↑	Minor neurological deficit ↑ Seizures ↑ Microcephaly ↑
Blackmon 2016	29 F, 101 M	2–35y	high and low	MRI, neurological assessment	Mild nonspecific neuroimaging abnormalities: ASD F> ASD M, p=.03 Treatment resistant epilepsy: ASD F>ASD M, p=.02	Not compared	Non-specific neurological abnormalities ↑ Treatment-resistant epilepsy ↑
Bolton 2011	46 F, 104 M	mean 32.6y	high and low	Survey	Epilepsy: ASD > NT reference, p<.001; ASD F>ASD M, p<.05	Epilepsy ↑	Epilepsy ↑
Camp-dell 2014	ASD: 39 F, 161 M NT: 49 F, 98 M	Asses-ment at age 2y	high and low	Data from medical records	Head circumference: ASD F= NT F, p=n.s.; ASD M>NT M, p<.05	No differences	Enlargement of head circumference ↓
Lainhart 1997	ASD: 21 F NT: 90 F	3–38y, mean 13.8y	?	Neurological examination	Neurological examination, head circumference: ASD group > references, p<.001; ASD F> ASD M (p value not told)	Macrocephaly ↑	Macrocephaly ↑

MRI= magnetic resonance imaging

Supplementary Table 11. Brain structure and functioning.

Article (first author and year)	**Participants**			**Methods**	**Results**		
	Number of participants	**Age**	**Functi-oning of ASD participants**		**Results of measurement**	**ASD females compared to NT females**	**ASD females compared to ASD males**
Beacher 2012a	ASD (AS): 13 F, 15 M NT: 15 F, 15 M	20–42y	high	MRI	White matter volume: ASD F < ASD M, p<.006; ASD F>NT F, p=.02.; ASD M=NT M, p=n.s.; NT F < NT M, p<.001, dg x sex interaction p=.01, n^2=.12 Gray matter at right inferior parietal lobe and rolandic operculum: ASD F = ASD M, p=n.s.; ASD F=NT F, p=n.s.; ASD M> NT M, p<.001, NT F < NT M, p<.001, dg x sex interaction p<.001, n^2=.31	White matter volume ↑	Enlargement of white matter ↑ Enlargement of gray matter at right inferior parietal lobe and rolandic operculum: ↓
Beacher 2012b	ASD (AS): 14 F, 15 M NT: 16 F, 16 M	mean 31.6y	high	fMRI (mental rotation, verbal fluency)	Activation during verbal fluency in left occipitoparietal and inferior prefrontal: ASD group > NT group, p<.05	Activation of left occipitoparietal and inferior prefrontal	No differences during verbal fluency Differences in

					Activity during mental rotation in occipital, temporal, parietal, middle frontal regions: ASD M, NT F> ASD F, NT M, p<.05	during verbal fluency ↑	activation during mental rotation
Bloss 2007	ASD: 9 F, 27 M NT: 14 F, 13 M	2–5y	high and low	MRI	Volume of whole brain, intracranial, cerebral gray cerebral white, cerebellar white, frontal gray, temporal gray: ASD F> NT F, p<.05; ASD M> NT M, p<.05 Volume of cerebellar gray and parietal white: ASD F> NT F, p<.05, ASD M=NT M, p=n.s. Volume of frontal white: ASD F = NT F, p=n.s.; ASD M> NT M, p<.05	Brain volume ↑ Cerebellar volume ↑ Parietal white matter ↑	No differences at brain enlargement Enlargement of cerebellar and parietal white matter↑ Enlargement of frontal white matter ↓
Caldero ni 2012	ASD: 38 F, Develop-mental delay: 38 F	2–8y	mainly low	MRI	Gray matter volume ASD F>NT F, p<.05	Gray matter volume ↑	Not comparable
Coffma n 2015	ASD: 12 F, 14 M	8–14y	high	EEG	Face vs houses: ASD M have differential N170 amplitude to faces vs houses but ASD F not have Faces vs inverted faces: ASD M have differential N170 amplitude to faces vs inverted faces but ASD F not have	Not comparable	Discrimination of faces to houses/inverted faces (N170) ↓
Craig 2007	ASD: 14 F NT: 19 F	ASD mean 35.0y, NT mean 37.9y	high	MRI	Gray matter density in temporal lobes, orbitofrontal cortex, right medial occipital lobe, left frontal right lobe and white matter density bilaterally anterior temporal lobes and brain stem: ASD F<NT F, p<.01 White matter density in association and projection fibers of the frontal, parietal, posterior temporal and occipital lobes, commissural fibers of the corpus callosum and cerebellum: ASD F> NT F, p<.01	Gray matter density ↓ White matter density ↑	Not comparable
Ecker 2017	ASD: 49 F, 49 M NT: 47 F, 51 M	18–42y	high	MRI	Neuroanatomical male brain type based on cortical thickness: ASD F> NT F, p<.001, ASD M=NT M Abnormality of cortical anatomy at bilateral parahippocampal areas, enthorinal cortex, inferior middle temporal lobe: ASD F> ASD M, p<.001	Abnormal gender coherence of neuroanatomy ↑	Abnormality of cortical anatomy ↑
Kirkovs ki 2016	ASD (23 AS, 4 HFA): 14 F, 13 M NT: 12 F, 11 M	19–56y	high	fMRI (ToM)	Activity of right posterior superior temporal sulcus: ASD F = NT F; ASD M < NT M, p=.004	No differences	Atypical decreased activity ↓
Lai 2013	ASD: 30 F, 30 M NT: 30 F, 30 M	18–49y	high	MRI	White matter at bilateral temporo-parieto-occipital regions (corpus callosum, bilateral cinglumun, inferior longitudinal fasciculus) and right arcuate fasciculus: ASD F > NT F; ASD M=NT M (p value not told) White matter at internal capsule	White matter at tempro-parieto-occipital regions ↑ White matter at internal capsule bilaterally ↓	Different abnormality in volume of white matter at many brain areas

					bilaterally at the level around basal ganglia and thalamus: ASD F< NT F; ASD M > NT M (p value not told)		
Piven 1996	ASD: 9 F, 29 M NT: 16 F, 20 M	12–29y, mean 18.0y	high and low	MRI	Volume of parietal, temporal, frontal lobe: ASD F= NT F, p=n.s.; ASD M> NT M, p<.05, ASD M>ASD F	No differences	Enlargement of parietal, temporal, frontal ↓
Retico 2016	ASD: 38 F, 38 M NT: 38 F, 38	1.8–7.4y	high and low	MRI	Gray matter volume: ASD F> NT F, p=.018; ASD M>NT M, p=.043 Gray matter in bilateral frontal lobes, anterior cingulate cortex, right cerebellum: ASD F> NT F Gray matter volume in the middle occipital gyrus, superior temporal gyrus: ASD M>NT M White matter volume ASD F> NT F, p=.017; ASD M>NT M, p=.023 Intracranial volume: ASD F> NT F, p=.016; trend level ASD M>NT M, p=.052	Gray matter volume in bilateral frontal lobes, anterior cingulate cortex, right cerebellum, white matter volume, intracranial volume ↑	Enlargement of gray matter in different brain areas Slightly more enlargement of white matter and intracranial volume ↑
Schaer 2015	ASD: 53 F, 53 M NT: 51 F, 53	8.8–25.6y	high	MRI	Cortical volume, volume of cerebral white, subcortical volume: ASD group = NT group; p=n.s.; all Females < all males, p<.001, not significant sex x dg interaction Gyrification of the ventromedial/orbitofrontal prefrontal cortex: ASD F= NT F = NT M > ASD M, p<.05	No differences at cortical volume	Cortical, cerebral white and subcortical volume ↓ (Similar difference than among NT) Abnormality in gyrification ↓
Scheider 2013	ASD: 13 F, 15 M NT: 13 F, 15 M	18–55y	high	fMRI (emotional pictures)	Bilateral medial frontal gyrus activation during empathy task: ASD F<ASD M, p<.05 NT F=NT M, p=n.s. Left amygdala activation during empathy task: ASD F<NT F, p<.05. p=n.s.; ASD M=NT M, p=n.s.	Left amygdala activation during empathy task ↓	Bilateral medial frontal gyrus activation during empathy task ↓
Schumann 2010	ASD: 9 F, 32 M NT: 12 F, 32 M	1–4y	mainly low	MRI	White and gray matter enlargement in frontal, temporal and cingulate cortex: ASD group > NT group; ASD F> ASD M	White and gray matter enlargement ↑	White and gray matter enlargement ↑
Schumann 2009	ASD: 9 F, 132M NT: 11 F, 28 M	1.5–5y	mainly low	MRI	Left amygdala volume: ASD F> NT F; p=.008, ASD M> NT M trend level, p=.08 Right amygdala volume: ASD F> NT F, P=.001, ASD M> NT M, p=.014	Amygdala volume ↑	Amygdala volume ↑
Sparks 2002	ASD: 7 F, 38 M NT: 8 F, 18 M	3.2–4.5y	low	MRI	Volume of cerebrum: ASD F >NT F, p=.01; ASD M>NT M, p=.001 Volume of cerebellum, hippocampus, amygdala: ASD F= NT F, p=n.s. ASD M > NT M, p≤.05	Cerebrum volume ↑	No differences at cerebrum volume Enlargement of cerebellum, hippocampus, amygdala ↓
Supekar 2015	ASD: 25 F, 25 M NT: 19 F, 19 M	7–13y	high	MRI	Total gray matter volume: ASD F= ASD M, P=n.s. Volume of gray matter in left motor cortex, left supplementary motor	No differences	Differences at volume in motor areas and amygdala

					area, cerebellum, fusiform gyrus, amygdala between ASD F - ASD M, p<.001, NT F = NT M		
Tepest 2010	ASD: 11 F, 18 M NT: 11 F, 18 M	20.9 – 53.3y	high	MRI	Total brain volume: All females < all males, p=.003; ASD F = NT F, p=n.s.; ASD M=NT M, p=n.s. Corpus callosum volume: ASD group= NT group, p=n.s.; ASD	No differences	Total brain volume ↓ (Similar difference than among NT)

MRI= magnetic resonance imaging EEG= electroencephalography, fMRI= functional magnetic resonance imaging

Supplementary Table 12. Brain connectivity.

Article (first author and year)	**Participants**			**Methods**	**Results**		
	Number of participants	**Age**	**Functioning of ASD participants**		**Results of measurements**	**ASD females compared to NT females**	**ASD females compared to ASD males**
Alaerts 2016	ASD: 42 F, 42 M NT: 75 F, 75 M	7–30y	high	fMRI (resting state)	Functional hyperconnectivity with right SFG/SMG and inferior frontal gyrus, with mid cingulum, left parahippocampal gyrus, right SFG/SMG and cerebellum, with right SFG/middle frontal gyrus, left MGF and right middle oribital gyrus, ASD F>NT F No connectivity differences between ASD F–ASD M	Functional hyper-connectivity ↑	No differences
Beacher 2012a	ASD: 13 F, 15 M NT: 15 F, 15 M	20–42y	high	DTI	Mean diffusivity in thalamus: ASD group < NT group, p=.01, n^2=.11, no sex x dg interaction FA in corpus callosum body: ASD F = ASD M, p=n.s.; ASD F=NT F, p=n.s.; ASD M<NT M, p=.02, NT F < NT M, p=.01, dg x sex interaction p=.003 FA right and left cingulum: ASD F = ASD M, p=n.s.; ASD F=NT F, p=n.s.; ASD M<NT M, p=.04, NT F < NT M, p=.003, dg x sex interaction p=.01 FA right and left corona radiate: ASD F = ASD M, p=n.s.; ASD F=NT F, p=n.s.; ASD M<NT M, p=.02, NT F < NT M, p<.001, dg x sex interaction p=.008	Mean diffusivity in thalamus ↓	FA abnormalities ↓ No differences in thalamus diffusivity
Kirkovski 2015	ASD (21 AS, 4 HFA): 13 F, 12 M NT: 12 F, 12 M	19–56y	high	DTI	FA, mean diffusivity, radial diffusivity, or axial diffusivity: ASD group = NT group, all F = all M; ASD F = NT F; ASD M=NT M, all p=n.s.	No differences	No differences
Nordahl 2015	ASD: 27 F, 112 M NT: 29 F, 53 M	2–4y	mainly low	DTI	Cortical projections in orbitofrontal cortex: ASD F > ASD M, p=.02; ASD F= NT F, p=n.s.; ASD M<NT M, p=.02, NT F = NT M, p=n.s. Cortical projections in anterior frontal cortex: ASD F<ASD M, p=.01; ASD F< NT F, p=.01, trend level ASD M > NT M, p=.09; trend level NT F>NT M, p=.08 Cortical projections in superior frontal cortex: ASD F= ASD M, p=n.s.; ASD F<NT F, p=.01, trend level ASD M <NT M, p=.07; NT F=NT M Cortical projections in posterior parietal	Mean, axial and radial diffusivity ↑ Cortical projections in anterior frontal cortex, superior frontal cortex and posterior parietal cortex ↓	Cortical projections in orbitofrontal cortex ↑ Cortical projections in anterior frontal cortex and posterior parietal cortex ↓

					cortex: ASD F <ASD M, p=.01; trend level ASD F< NT F, p=07, ASD M= NT M, p=n.s.; NT F = NT M, p=n.s. Mean, axial and radial diffusivity: ASD F> NT F; ASD M = NT M		
Zeestraten 2017	ASD: 37 F, 16 M NT: 54 F, 61 M	18–52y	high	DTI	FA frontal tracts: ASD F=NT F, p=n.s.; ASD M<NT M, p<.05, Significant dg x sex effect, suggesting that ASD dg effect in males is significantly different than ASD dg effect in females.	No differences	Frontal connectivity abnormalities ↓

M= male, F=female, ASD=autism spectrum disorder, NT=Neurotypical, FA=Fractional anisotropy, DTI=diffusion tensor imaging, fMRI= functional magnetic resonance imaging

Supplementary Table 13. Genetic burden

Article (first author and year)	**Participants**	**Methods**	**Results**
Jacquemont 2014	109 females and 653 males with ASD	Copy number variants analysis	Females with ASD showed increase in large CNVs compared to males with ASD, p=.003
Levy 2011	915 families	Mapping, Copy number variants analysis	De novo events: ASD F>ASD M, p=.16, de novo events are also more frequently deletions in ASD females than ASD males, p=.04 CNV: ASD F> ASD M (11.7% vs 7.4%,) Genes that have de novo events: ASD F>ASD M, p=.05
Palmer 2017	3166542 children: 1547266 females, 1619174 males	Assessment of ASD recurrence	Recurrence when ASD child is female: 7.6% of female siblings, 16.7% of male siblings Recurrence when ASD child is female: 4.2% of female siblings, 12.9% of male siblings
Taniai 2008	45 twin pairs with at least one siblings have ASD	Heritability estimation (ASD traits evaluated by CARS)	Heritability for females0.87 Heritability for males 0.73

CARS= Childhood Autism Rating Scale, CNV = copy number variants

Supplementary Table 14. X-chromosome.

Article (first author and year)	**Participants**	**Methods**	**Results**
Gong 2008	182 ASD females, 621 mothers of ASD child, 209 NT females	X inactivation analysis	No significant excess of X skewedness, but there was subgroup that have skewed inactivation and ASD associated genes in X-chromosome
Gockley 2015	4709 families with ASD child	Identification of SNPs in X chromosome that escape inactivation, identification SNPs in X-chromosome	No specific SNPs found
Talebizadeh 2005	30 females with ASD, 35 NT females	X inactivation analysis	X chromosome skewness in females: ASD F > NT F (significant, p value not told)

Supplementary Table 15. Association and linkage studies.

Article (first author and year)	**Participants**	**Methods**	**Results**
Cantor 2005	91 families with 109 sibling pairs with ASD	Genome wide linkage scan	Male only linkage 17q11-17q21
Carayol 2011	179 females and 664 males with ASD	Association analysis (case-pseudocontrol)	Female only associations: MARK1 (1q41), ITGB3 (17q21) Male only associations: ATP2B2 (3p25), PITX1(5q31.1), HOXA1 (7p15.2) Both females and males associations: CNTNAP2 (7q35-36), EN2 (7q36.3), JARID2 (6p22)
Chakraborti 2016	203 ASD, 236 NT	Case-control association analysis	Both female and male association: MAOB (Xp11.3) (genotype CC at rs2283728 and rs2283727), but only male association correlate with symptom severity and serotonin level

Chakrabarti 2009	174 ASD (A/AS), 349 NT	Case-control study, ASD traits association study (measured by AQ and EQ)	Female only association: MAOB (Xp11.3), NLGN4X (Xp22.32-31) Both female and male associations: CYP11B1 (8q21), CYP17A1 (10q24.3), CYP19A1 (15q21.2), ESR2 (14q23.2), HOXA1 (7p15.3), NTRK1 (1q21-22), ARNT2 (15q24), WFS1 (4p16), OXTR (3p25.3), OXT (20p13), AVPR1B (1q32.1)
Chang 2013	801 families with ASD child	Genome-wide association study	Male only association 13q33.3, pseudoautosomal boundary Xp22.33/Yp11.31
Gong 2008	182 ASD females, 621 mothers of ASD child, 209 NT females	Linkage analysis of subgroup of participants	Among the subgroup of females where X skewedness was high (>80:20), there was linkage Xq27-Xq28
Henningson 2009	267 ASD and 118 parents and 32 affected siblings, 617 NT	Case-control association analysis, Family-based association study, Transmission disequilibrium analysis	Female only association: AR (Xp12) short CAG alleles as well as of the A allele of the rs6152 SNP Disequilibrium test at AR: association with the GGN polymorphism, the rare 20-repeat allele is undertransmitted to male cases and the 23-repeat allele is overtransmitted to female cases.
Hu 2015	5 females and 4 males with ASD, 8 NT females, 9 NT males	Protein immunoflueren ce analysis on the post-mortem frontal cortex	RORA protein expression in frontal cortex: effects size suggests and trend level NT F> NT M, ASD F=ASD M
Lamb 2005	420 individuals with ASD, 219 siblings pairs	Linkage analysis	Male only linkage 16p Both female and male linkage 15q
Mitra 2016	6762 family with ASD, 1884 cases, 1504 controls (from different datasets)	Genome wide association analysis	Female only associations: CTNNA2/SUCLG1 (2p11-2p12), CSMD1(8p23.2) Male only associations: EXT1 (8q24.11), HDGFL1/NRSN1 (6p22.3), SPANXC (Xq27.2), PRR32/ACTRT1 (Xq25), MAGEC2/SPANXN4 (Xq27.2-Xq27.3) Both female and male associations: ZNF677 (19q13.42), EXOC4 (7q33),), PRKX(Xp22.33), NLGN4X (Xp22.31) Several anthropometric heterogeneous (AH) (e.g. BMI, heights, weight, hip, waist) SNPs were associated with ASD, all p<.05
Schellenber g 2006	222 families at least one ASD child, together 996 individuals in which 399 ASD individuals	Genome wide linkage scan	Female only linkage: 4 (111.41cM) Male only linkage: 11 (83.82cM) Female and male linkage but stronger in male: 7 (133.16cM) Female and male linkage: 10 (0-13.2cM), 15 (86-106cM), 19 (10.9cM)
Schuch 2016	39 females and 170 males with ASD and their biological parents	Family-based association analyses	Male only association: SLC6A4 (17q11.2) rs1042173 GG genotype associated with psychomotor agitation
Stone 2004	257 nuclear families with two or more ASD children	Complete genome linkage scan	Male only linkage 17q11
Szatmari 2007	1,496 ASD families (7,917 family members)	Linkage analysis	Male linkage 5q12.3, 9q33.3 Female and male linkage 5p15.33, 9p24.1, 11p12-13
Verma 2014	421 ASD, 227 NT	Association analysis	Male association: MAOA (Xp11.3) rs6323
Werling 2014	1008 ASD multiplex families	Genome wide association analysis	Male only linkage 1p31.3 Female and male linkage: 8p21.2, 8p12
Yu 2011	229 ASD, 184 NT	Case-control association analysis	Male association: NLGN3 (Xp13.1)

Supplementary Table 16. Testosterone.

Article (first author and year)	**Participants**		**Results**	
	Number of participants	**Age**	**Results of measurements**	**ASD females compared to NT females**
Bejerot 2012	ASD: 24 F, 26 M NT: 26 F, 28 M	20–47y	Serum mean TT: ASD F> NT F, p<.05; ASD M=NT M; p=.n.s. Serum bioactive TT: ASD F> NT F, p<.05; ASD M=NT M; p=.n.s. Gender coherence of face features gender coherence (evaluated by group of assessors): ASD F<NT F, p.<.001; ASD M<NT M; p<.001 Gender coherence of voice coherence (evaluated by group of assessors): ASD F<NT F, p.<.01; ASD M<NT M; p<.001 Masculinized digit ratio 2D:4D: ASD F= NT F, p=n.s.; ASD M< NT M, p<.05	Medium TT levels ↑ Bioactive TT levels ↑ Masculinization of facial features and voice ↑

Geier 2007	ASD: 11 F, 59 M	6–27 y, mean 10.8y	Serum mean TT: ASD F, ASD M> reference ranges, p<.001; ASD F > ASD M, (significant but p-value not told) Serum free TT: ASD F, ASD M> reference ranges, p<.00; ASD F > ASD M, (significant but p-value not told) Serum DHEA: ASD F, ASD M> reference ranges, p<.001 Serum androstenedione: ASD F, ASD M> reference ranges, p<.001	Mean TT levels ↑ Serum free TT ↑ Serum DHEA ↑
Ingu-domnukul 2007	ASD (50 AS, 3HFA, 1 PDD-NOS): 54 F, NT: 183 F, Mothers of ASD child: 74	19–63y	TMQ Polycystic ovary syndrome, unusually painful periods, tomboyism: ASD F>NT F, p<.05 TMQ delayed puberty: ASD F>NT Fp<.01 TMQ hirsutism, irregular menstrual cycle, bisexuality, asexuality: ASD F>NT F,p<.001 TMQ severe acne: ASD F> NT F, p<.001; mothers of ASD child > NT, p<.05	Hirsutism ↑ Bisexuality ↑ Asexuality ↑ Irregular menstrual cycle ↑ Dysmenorrhea ↑ Polycystic ovary syndrome ↑ Severe acne ↑ Tombyism ↑
Pohl 2014	ASD: 415 F, NT: 415 F	24–52y	TMQ irregular menstrual cycle, polycystic ovary syndrome, gender dysphoria, tomboyism, transgender, asexualism, bisexualism: ASD F> NTF, p<.001 TMQ precocious puberty, early growth spurt, severe acne: ASD F> NT F, p<.01	Irregular menstrual cycle ↑ Polycystic ovary syndrome ↑ Severe acne ↑ Early growth spurt ↑ Precocious puberty ↑ Gender dysphoria ↑ Tomboyism ↑ Transgender ↑ Asexualism ↑ Bisexualism ↑
Schwarz 2011	ASD (45 AS): 23 F, 22 M NT: 24 F, 26 M	adults	Estimated free androgen index (from blood serum sample): ASD F>NT F, p<.05	Free androgen index ↑
Steeb 2014	ASD (30 AS): 16 F, 14 M NT: 16 F, 13 M	22–40y	Estimated free androgen index (from blood serum sample): ASD F> NT F, p=.00275 (ASD F increased ratio of 1.63), ASD M= NT M, p=n.s.	Free androgen index ↑

DHEA = dehydroepiandrosterone,, TMQ: Testosterone-related Medical Questionnaire, TT=Testosterone

Supplementary Table 17. Oxytocin and vasopressin.

Article (first author and year)	**Participants**		**Results**	
	Number of participants	**Age**	**Results of measurements**	**ASD females compared to NT females and ASD males**
Miller 2013	ASD: 19 F, 21 M NT: 16 F, 19 M	8–18y	Oxytocin level at blood: Females all > males all, P=.033; ASD group = NT group, p=n.s. Vasopressin level at bloood: Females all < males all, p=.043; ASD group = NT group, p=n.s.	No differences compared to NT females. Oxytocin ↑ compared to ASD males. Vasopressin ↓ compared to ASD males.